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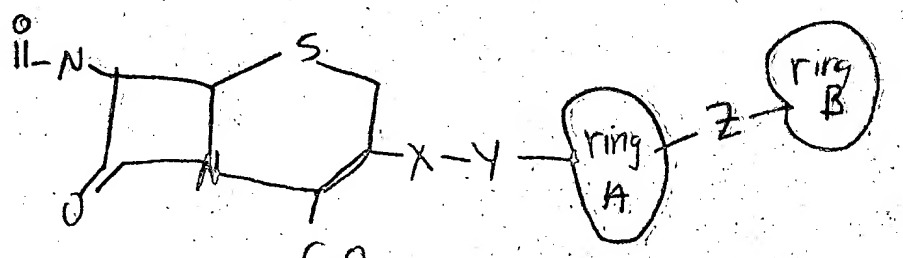
SEARCH REQUEST FORM

Requestor's Name: 847525 Serial Number: BERCH

Date: 3/13/02 Phone: 4718 LDIJ 4E12 Art Unit: 1624

Search Topic:

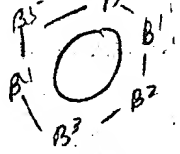
Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



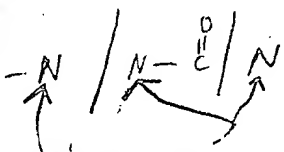
MARY

X = linker of 1-7 atoms of any type

Y = O/S/N

Ring A is  normalized ring. Cannot be all B = C/N fused

016 907-17

Z = O/ 

chain only

Ring B - same definition as ring A, but ring B cannot be phenyl 

STAFF USE ONLY

Date completed: 3/14
Searcher: Craig
Terminal time:
Elapsed time:
CPU time:
Total time: 9
Number of Searches:
Number of Databases:

Search Site
- STIC
- CM-1
- Pre-S

Type f Search
- N.A. Sequence
- A.A. Sequence 2
- Structure
- Bibliographic

Vendors
- IG Suite
- STN 206.59
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other

U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

63118

SEARCH REQUEST FORM

Requestor's Name: BERCH Serial Number: 847525

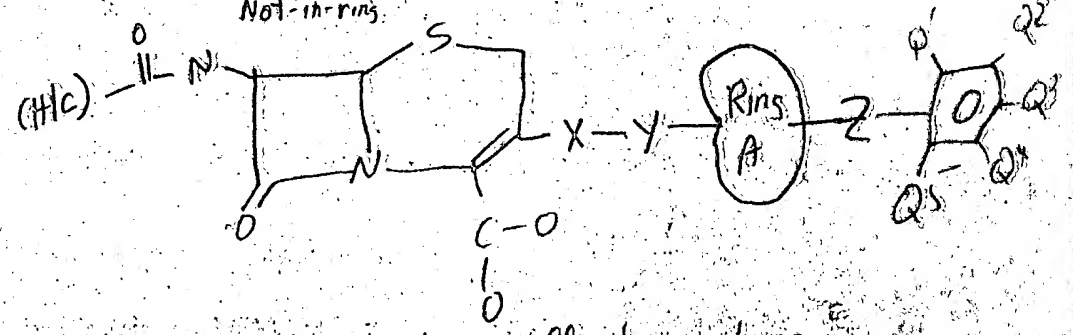
Date: _____ Phone: 4718 Art Unit: 1624

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

Z = O / C(=O) / C(=O)-N / N-C(=O) / N

Not-in-ring

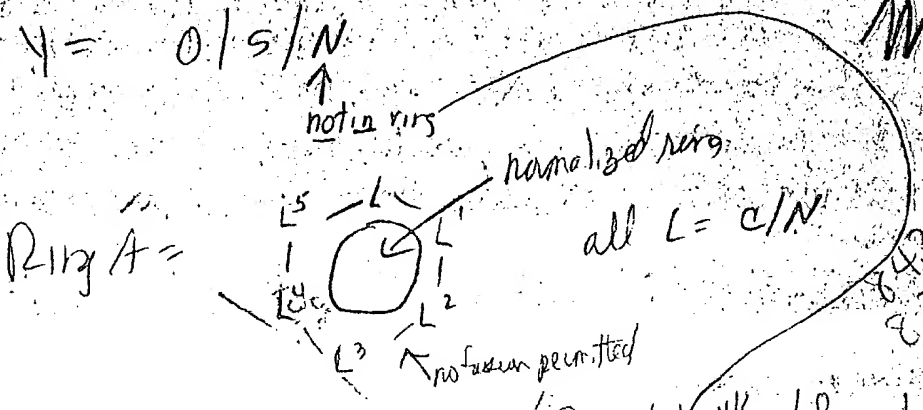


X = linker of 1-7 atoms, all chain-type

Y = O / S / N

not in ring

MAP



all Q = H / CN / NO2 / CF3 / C(=O)-H / N(H)C / C(=O)-CH3 / CH3

STAFF USE ONLY

Date completed: 7/27

Searcher: Mary

Terminal time: 9

Elapsed time: _____

CPU time: _____

Total time: _____

Number of Searches: _____

Number of Databases: _____

Search Site

_____ STIC

_____ CM-1

_____ Pre-S

Type of Search

_____ N.A. Sequence

_____ A.A. Sequence

1 Structure

_____ Bibliographic

Vendors

_____ IG Suite

258 STN

_____ Dialog

_____ APS

_____ Geninfo

_____ SDC

_____ DARC/Questel

_____ Other

PTO-1590 (9-90)

USCOMM-DC 90-3952

★ U.S.GPO: 1995-398-798/22489

U.S. DEPARTMENT OF COMMERCE

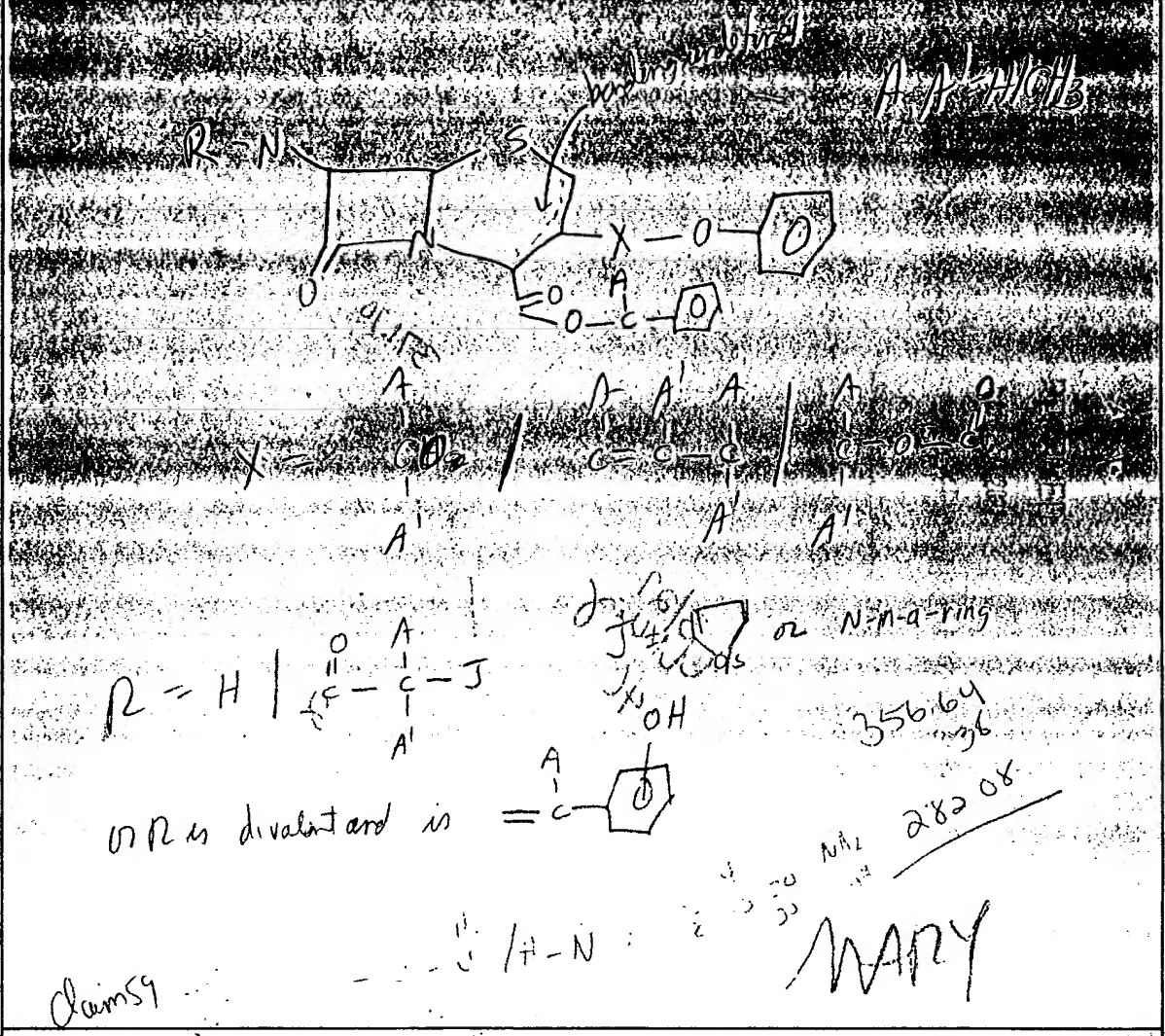
SEARCH REQUEST FORM

Requestor's Name: Brett Serial Number: 09/847525

Date: Phone: 30878 Art Unit: 1624

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors, keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).



STAFF USE ONLY

Date completed: 3/27

Searcher: Mary

Terminal time: 23

Elapsed time:

CPU time:

Total time:

Number of Searches:

Number of Databases:

Search Site

- STIC
- CM-1
- Pre-S

Type of Search

- N.A. Sequence
- A.A. Sequence
- Structure
- Bibliographic

Vendors

- IG Suite
- STN
- Dialog
- APS
- Geninfo
- SDC
- DARC/Questel
- Other

L5 0 L4

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COST IN U.S. DOLLARS

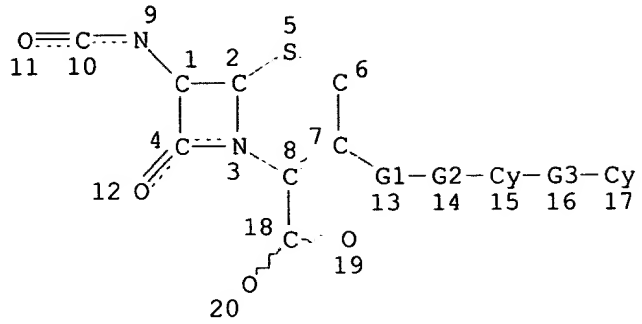
	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.32	206.59

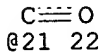
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

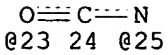
	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.44

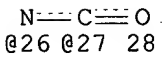
Beach
847525

=> d l4 que stat;d 1-17 ide cbib abs
L1 STR









REP G1=(1-7) A
VAR G2=O/S/N
VAR G3=O/21/23-15 25-17/26-15 27-17/N
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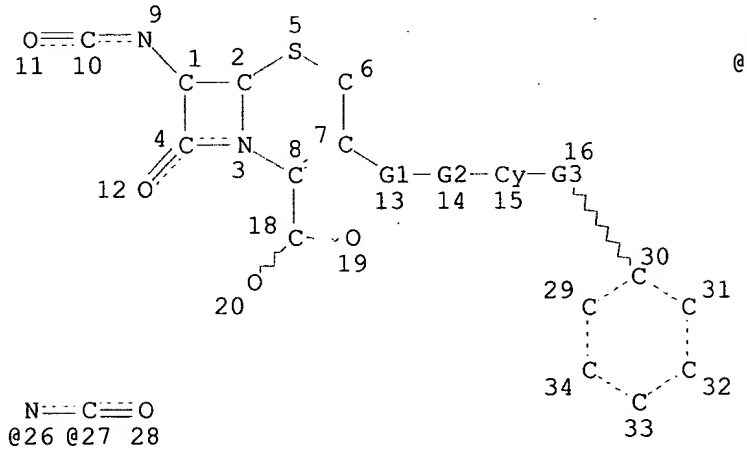
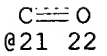
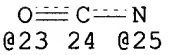
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 28

STEREO ATTRIBUTES: NONE
L2 STR







REP G1=(1-7) A
VAR G2=O/S/N
VAR G3=O/21/23-15 25-30/26-15 27-30/N
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

Searched by: Mary Hale 308-4258 CM-1 12D16

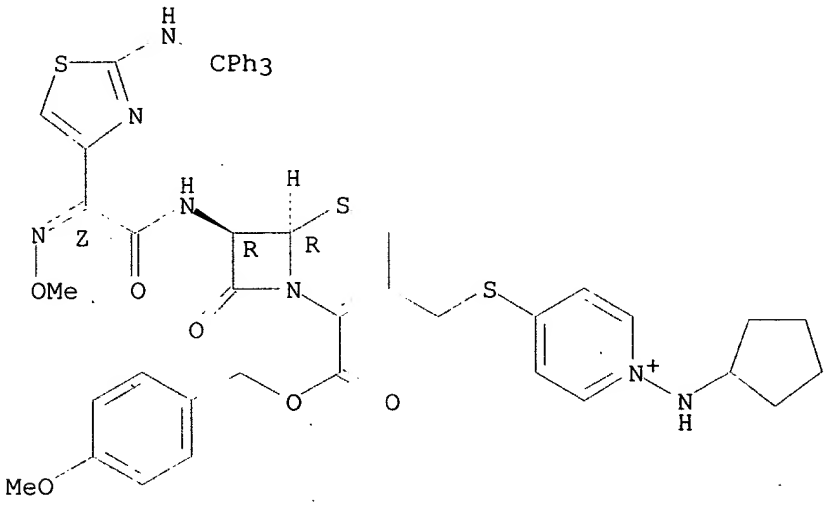
STEREO ATTRIBUTES: NONE
L4 17 SEA FILE=REGISTRY SSS FUL L1 NOT L2

100.0% PROCESSED 61917 ITERATIONS 17 ANSWERS
SEARCH TIME: 00.00.10

L4 ANSWER 1 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 153136-67-5 REGISTRY
CN Pyridinium, 1-(cyclopentylamino)-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C51 H50 N7 O6 S3 . I
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN:

Searched by: Mary Hale 308-4258 CM-1 12D16

0021-8820.

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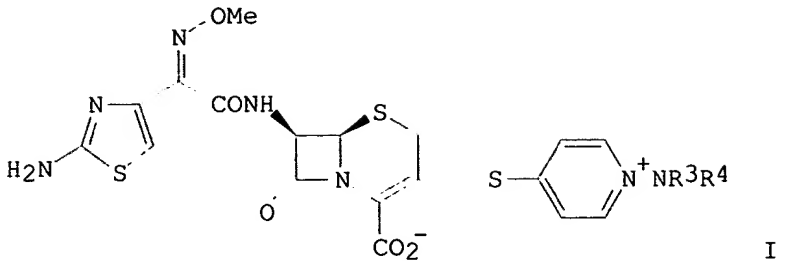

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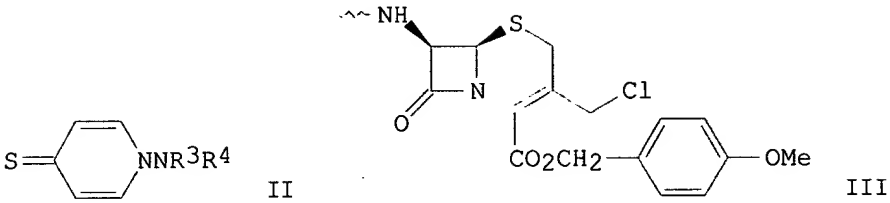


II III

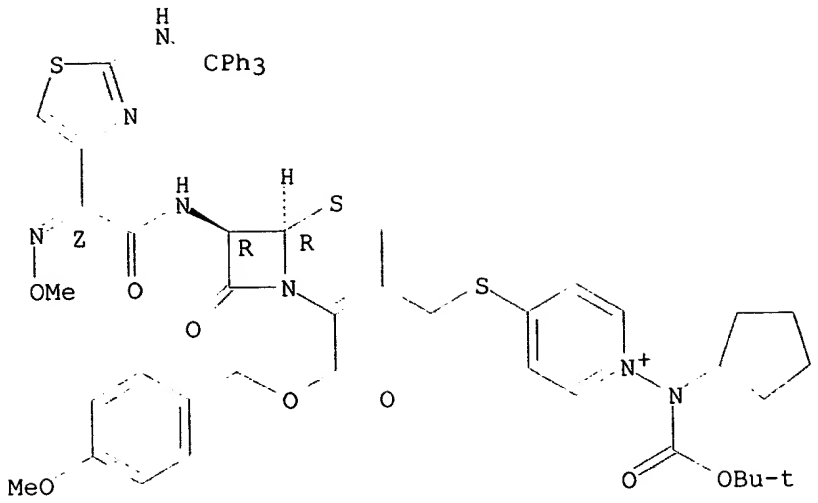
AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

L4 ANSWER 2 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134482-98-7 REGISTRY
CN Pyridinium, 1-[cyclopentyl[(1,1-dimethylethoxy)carbonyl]amino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C56 H58 N7 O8 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



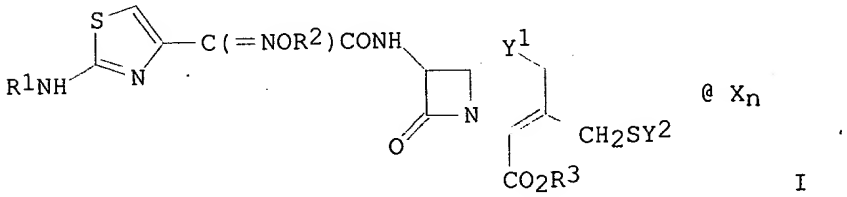
PAGE 2-A

● I^-

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:59084 Preparation of cephalosporins as antibacterial agents. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). PCT Int. Appl. WO 9114692 A1 19911003, 82 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB331 19910304. PRIORITY: GB 1990-6728 19900326.

GI



AB Title compds. I [R1 = H, amino protecting group; R2 = H, (substituted) C1-12 alkyl, (substituted) C3-7 cycloalkyl; R3 = removable carboxy protecting group; Y1 = S, SO, SO2; Y2 = (substituted) aminopyridinio; X = anion; n = 0, 1; with provisos] are prepd. as antibacterial agents (no data). 2-(2-Amino-4-thiazolyl-2-(Z)-(cyclopentyloxyimino)acetic acid in DMF was treated with (Me2CH)2NEt (II), cooled to -30.degree., treated with MeSO2Cl, recooled to -30.degree.. 4-Methoxybenzyl [6R,7R]-amino-3-(chloromethyl)ceph-3-em-4-carboxylate-HCl in DMF and II was added to the recooled soln. to give the thiazolylcephemcarboxylate which was treated with 1-(methylamino)-4-thiopyridone to give the pyridinium deriv. which was deprotected to give the title [6R,7R]-7-[2-(2-amino-4-thiazolyl-2-(Z)-(cyclopentyloxyimino)acetamido]-3-[1-(methylamino)pyridinio-4-

Searched by: Mary Hale 308-4258 CM-1 12D16

thiomethyl]ceph-3-em-4-carboxylate.

REFERENCE 2: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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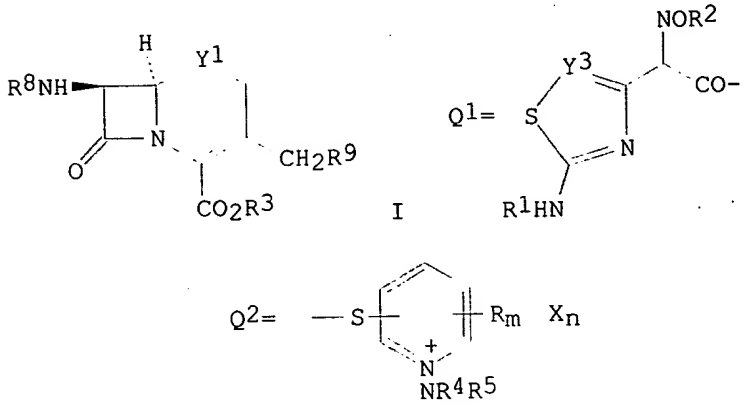


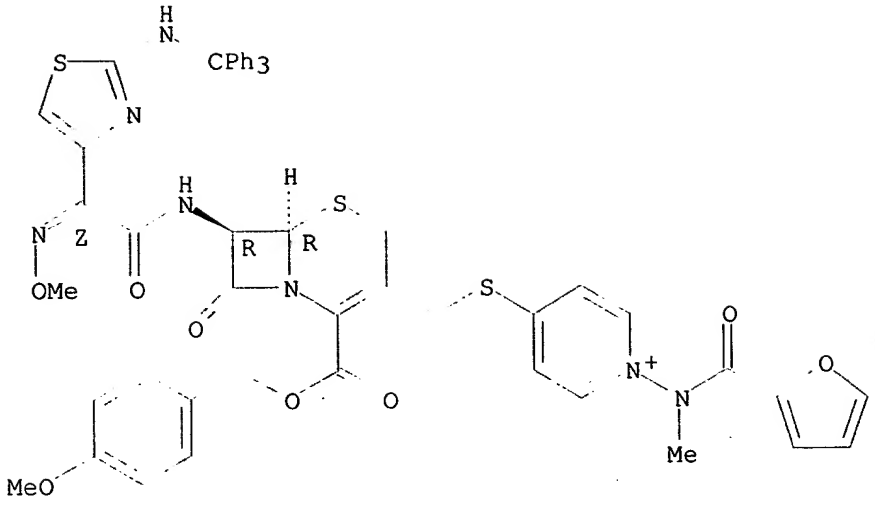
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L4 ANSWER 3 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134482-69-2 REGISTRY
CN Pyridinium, 1-[(2-furanylcarbonyl)methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C52 H46 N7 O8 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



PAGE 2-A

● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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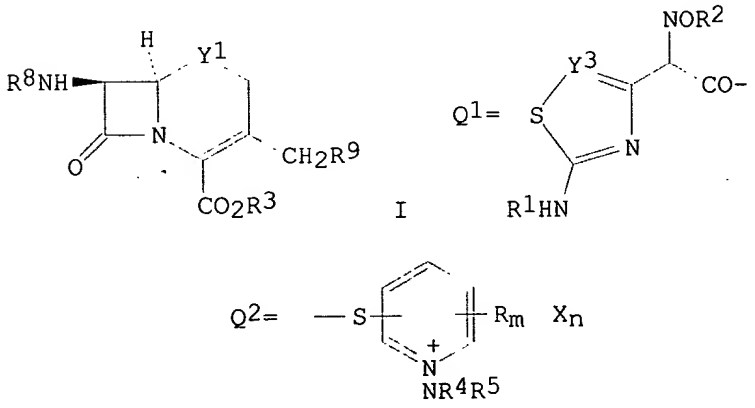


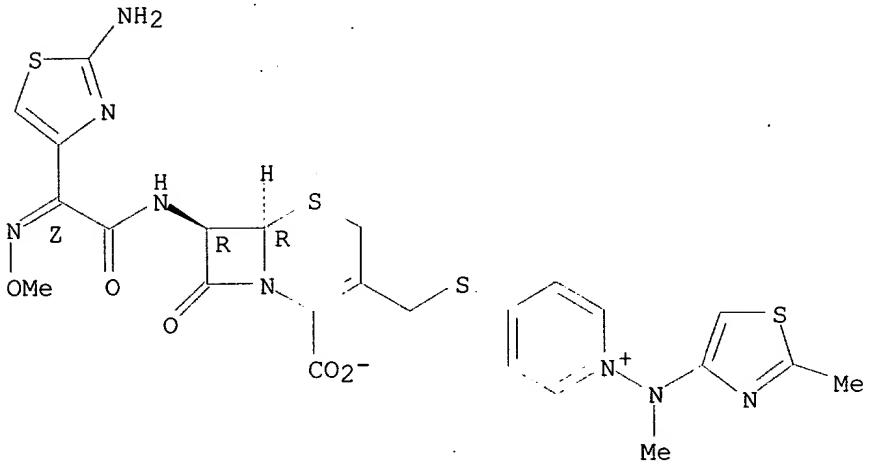
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.;

Searched by: Mary Hale 308-4258 CM-1 12D16

NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L4 ANSWER 4 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134481-90-6 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[methyl(2-methyl-4-thiazolyl)amino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H24 N8 O5 S4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

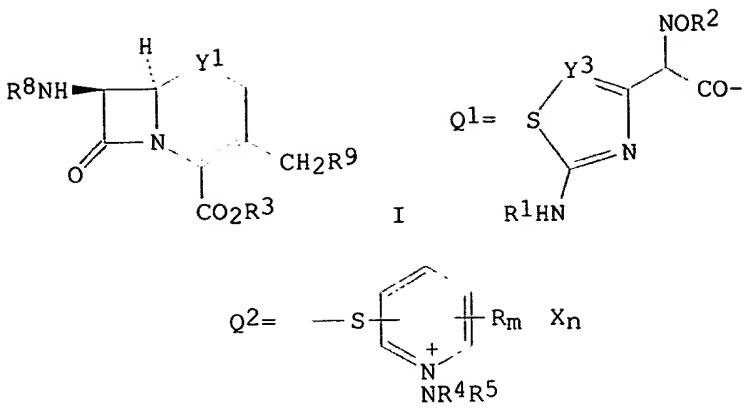


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

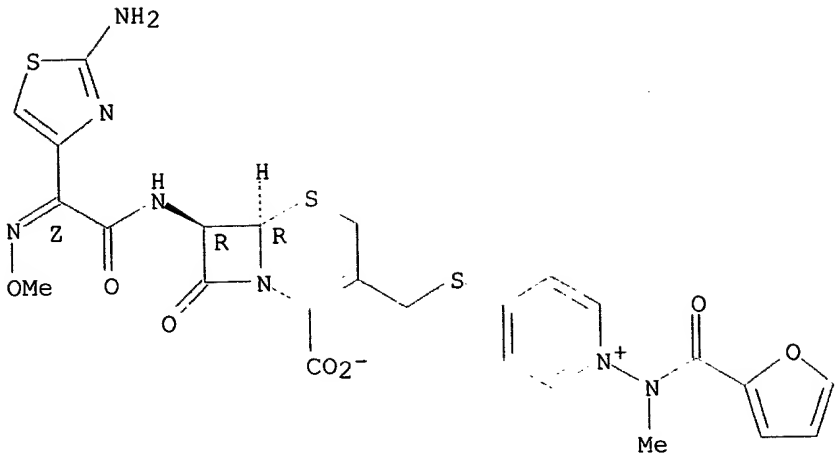


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L4 ANSWER 5 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134481-77-9 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(2-furanylcarbonyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H23 N7 O7 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

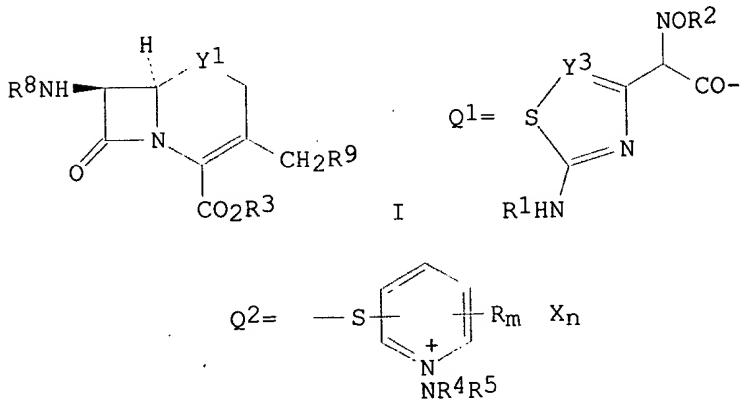
Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

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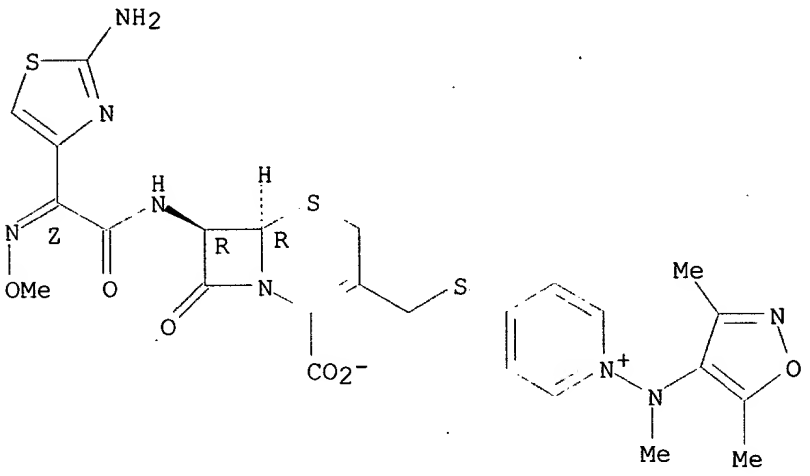
L4 ANSWER 6 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134481-67-7 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,5-dimethyl-4-isoxazolyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C25 H26 N8 O6 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

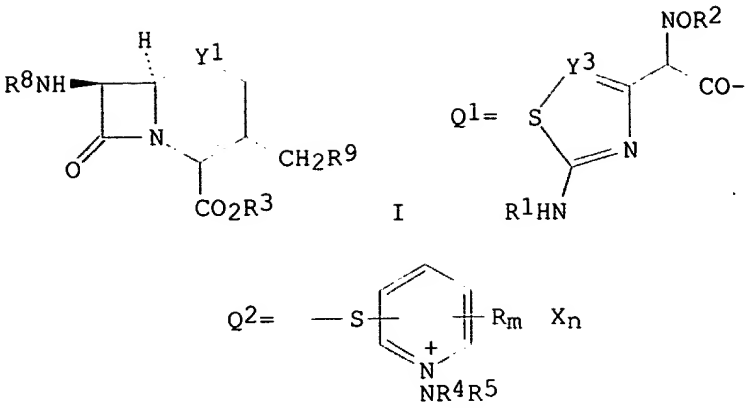


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

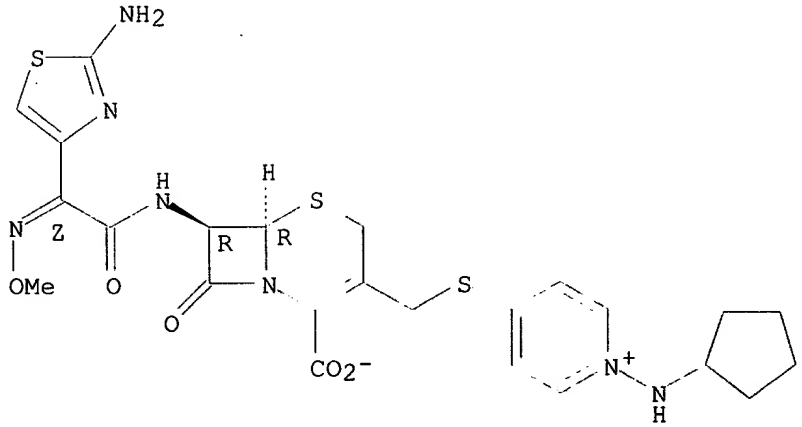
Searched by: Mary Hale 308-4258 CM-1 12D16



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L4 ANSWER 7 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134481-58-6 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(cyclopentylamino)-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C24 H27 N7 O5 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



3 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

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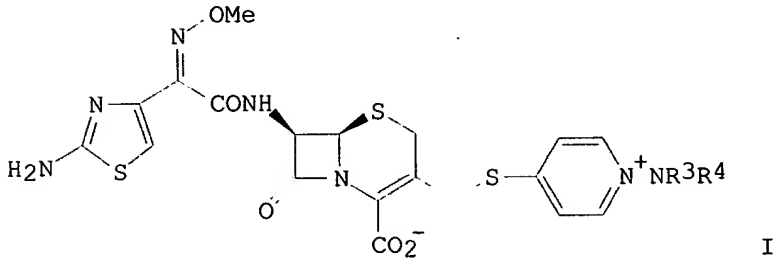
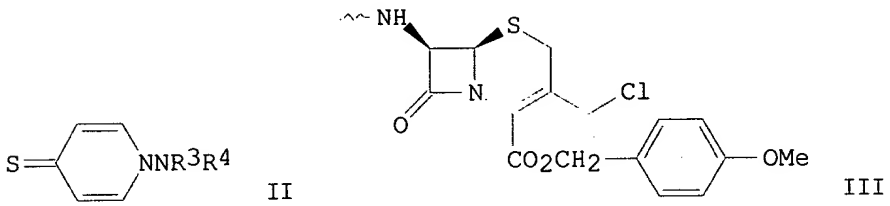


I



II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

REFERENCE 2: 116:59084 Preparation of cephalosporins as antibacterial agents. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). PCT Int. Appl. WO 9114692 A1 19911003, 82 pp. DESIGNATED STATES: W: JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1991-GB331 19910304. PRIORITY: GB 1990-6728 19900326.

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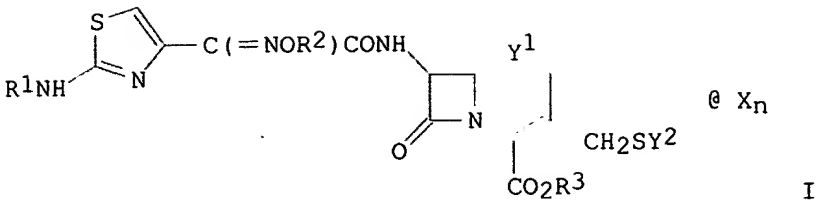

I

AB Title compds. I [R1 = H, amino protecting group; R2 = H, (substituted) C1-12 alkyl, (substituted) C3-7 cycloalkyl; R3 = removable carboxy protecting group; Y1 = S, SO, SO2; Y2 = (substituted) aminopyridinio; X = anion; n = 0, 1; with provisos] are prepd. as antibacterial agents (no data). 2-(2-Amino-4-thiazolyl-2-(Z)-(cyclopentyloxyimino)acetic acid in DMF was treated with (Me2CH)2NEt (II), cooled to -30.degree., treated with MeSO2Cl, recooled to -30.degree.. 4-Methoxybenzyl [6R,7R]-amino-3-(chloromethyl)ceph-3-em-4-carboxylate-HCl in DMF and II was added to the recooled soln. to give the thiazolylcephemcarboxylate which was treated with 1-(methylamino)-4-thiopyridone to give the pyridinium deriv. which was deprotected to give the title [6R,7R]-7-[2-(2-amino-4-thiazolyl-2-(Z)-(cyclopentyloxyimino)acetamido]-3-[1-(methylamino)pyridinio-4-thiomethyl]ceph-3-em-4-carboxylate.

REFERENCE 3: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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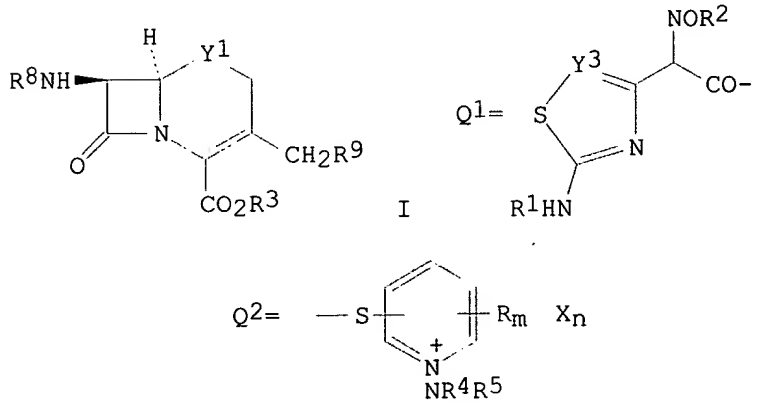

I

AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-

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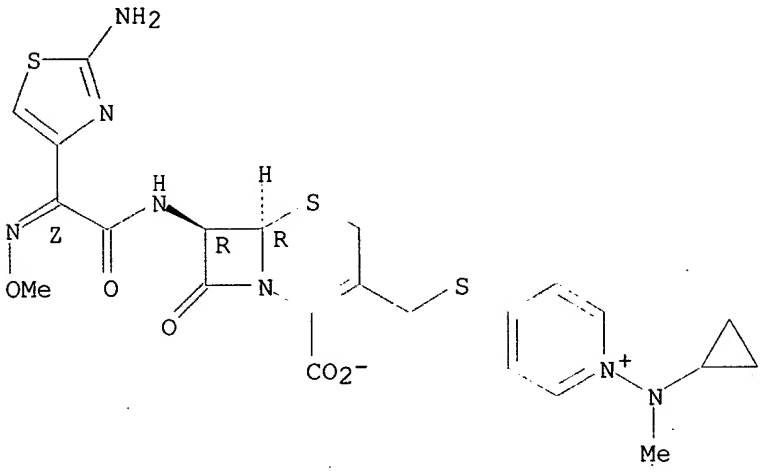
(dimethylamino)pyridinium-4-ylthio iodide].

L4 ANSWER 8 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134481-54-2 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(cyclopropylmethylamino)-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H25 N7 O5 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

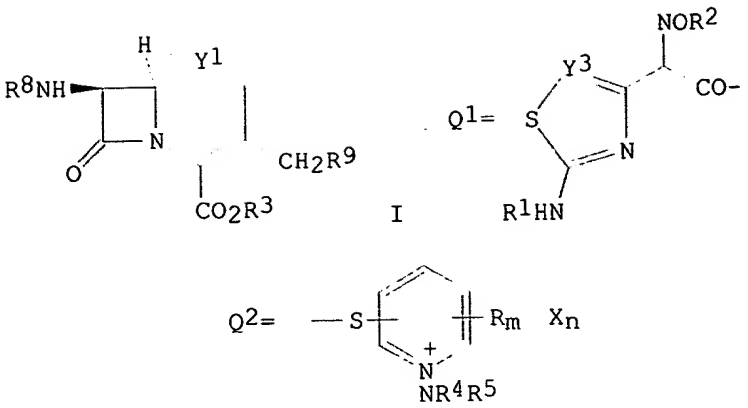


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

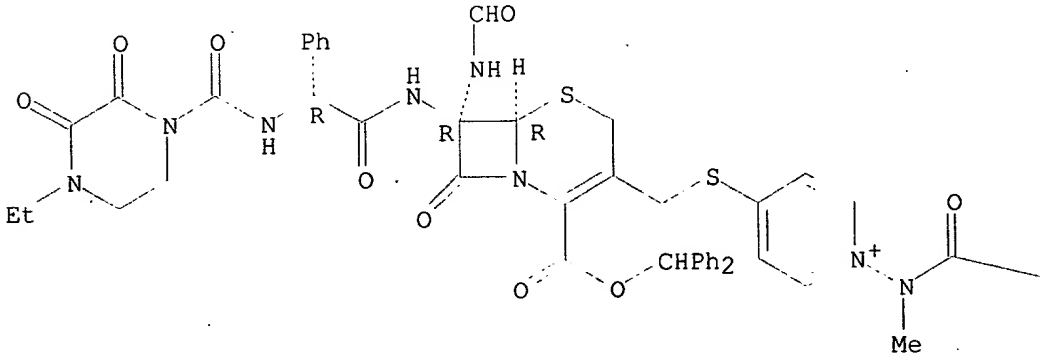


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

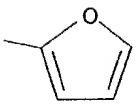
L4 ANSWER 9 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134368-53-9 REGISTRY
CN Pyridinium, 4-[[[2-[(diphenylmethoxy)carbonyl]-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(2-furanylcarbonyl)methylamino]-, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C48 H45 N8 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



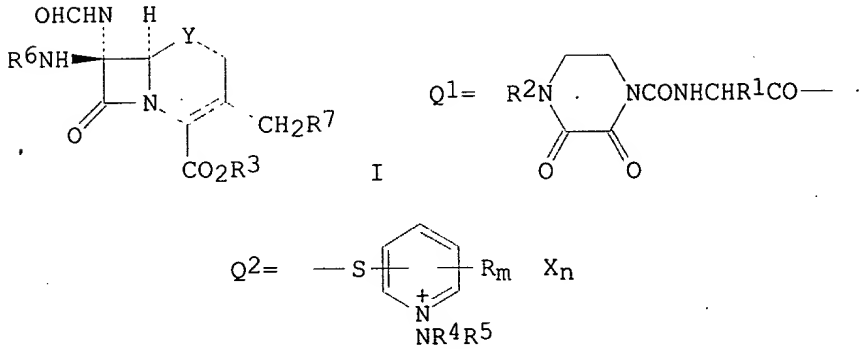
Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

GI



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

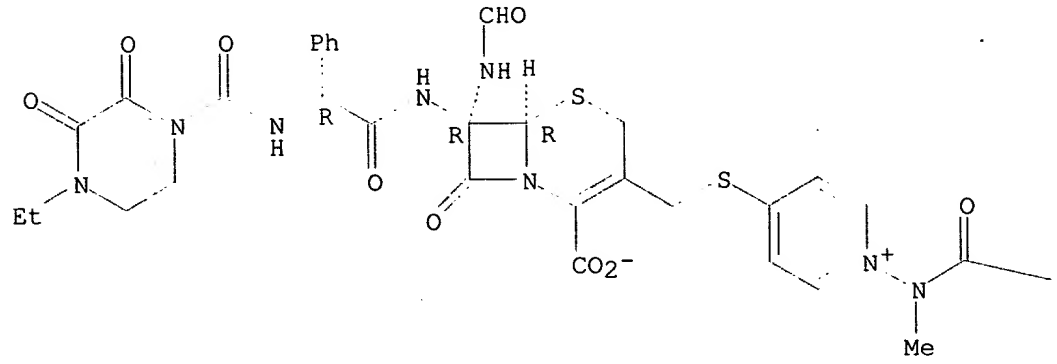
L4 ANSWER 10 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 134367-94-5 REGISTRY

Searched by: Mary Hale 308-4258 CM-1 12D16

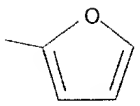
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(2-furanylcarbonyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H34 N8 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



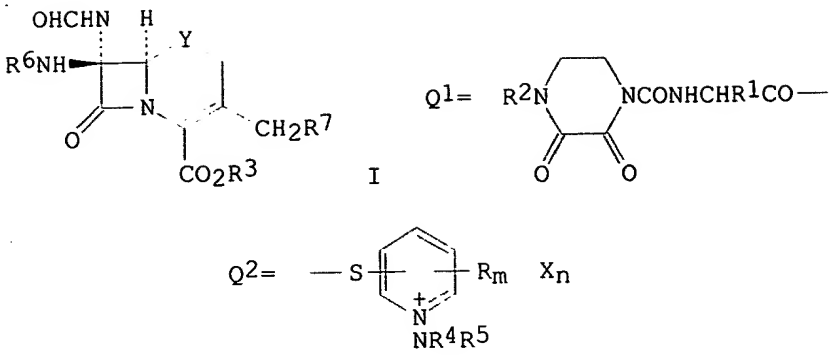
PAGE 1-B



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.
GI

Searched by: Mary Hale 308-4258 CM-1 12D16

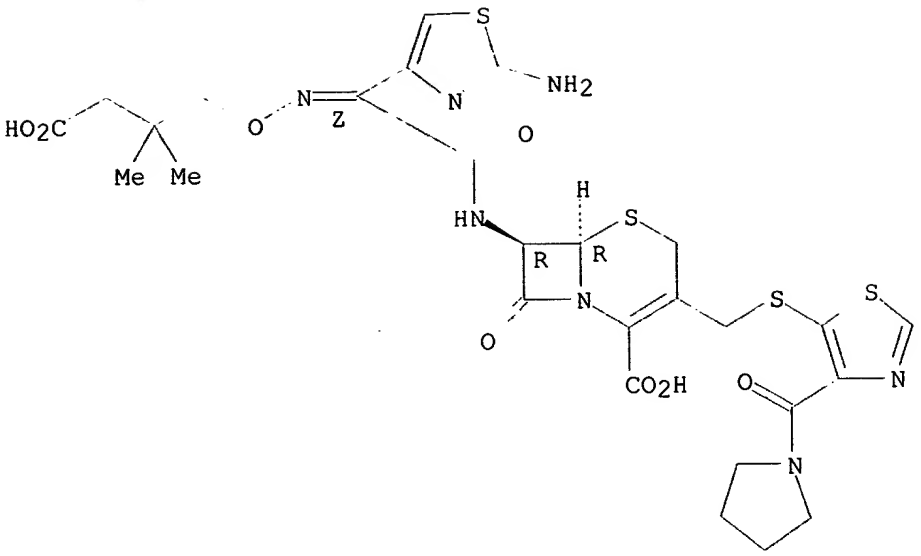


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

L4 ANSWER 11 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 133897-89-9 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)[(3-carboxy-2,2-dimethylpropoxy)imino]acetyl]amino]-8-oxo-3-[[[4-(1-pyrrolidinylcarbonyl)-5-thiazolyl]thio]methyl]-, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H31 N7 O8 S4
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

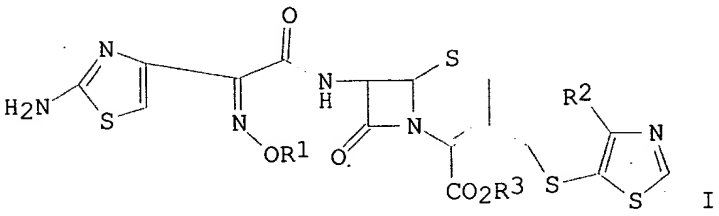


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 114:228629 Preparation of bis(thiazolyl) cephalosporins. Adam, Friedhelm; Duerckheimer, Walter; Scheunemann, Karl Heinz; Isert, Dieter; Seibert, Gerhard (Hoechst A.-G., Fed. Rep. Ger.). Eur. Pat. Appl. EP 409055 A1 19910123, 20 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1990-113195 19900711. PRIORITY: DE 1989-3923541 19890715.

GI



I

AB The title compds. [I; R1 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, etc.; R2 = H, CO2H, alkoxycarbonyl, carbamoyl; R3 = H, cation, easily cleavable ester group], were prepd. as antibacgerials (no data). Thus, 2-aminothiazol-4-yl-2Z-methoxy = iminoacetic acid in DMF was treated with hydroxybenzotriazole and DCC; after 4 h, dicyclohexylurea was filtered off and 7-amin-3-[(4-methoxycarbonyl-1,3-thiazol-5-yl)thiomethyl]ceph-3-en-4-carboxylic acid (prepn. given) was added followed by stirring for 10 h to give 75% I (R 1 = Me, R2 = CO2Me, R3 = H).

L4 ANSWER 12 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 133897-70-8 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

Searched by: Mary Hale 308-4258 CM-1 12D16

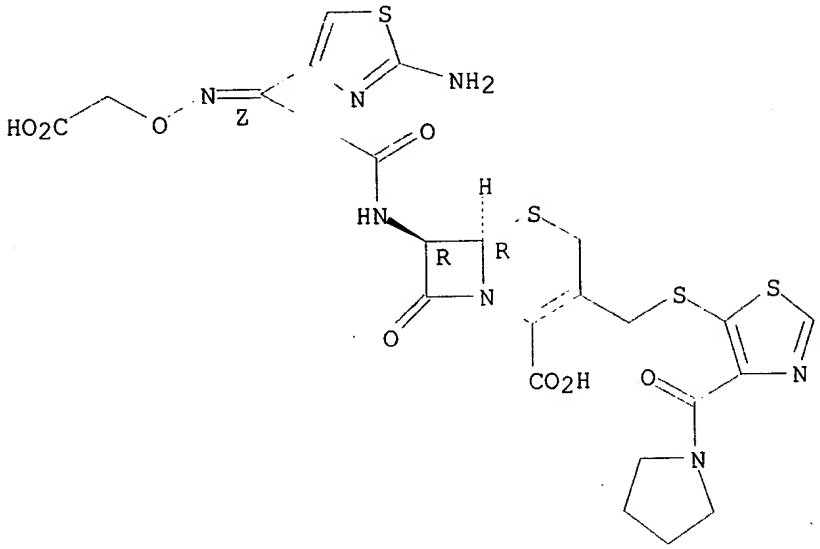
7-[[(2-amino-4-thiazolyl)[(carboxymethoxy)imino]acetyl]amino]-8-oxo-3-[[[4-(1-pyrrolidinylcarbonyl)-5-thiazolyl]thio]methyl]-, [6R-[6.alpha.,7.beta.(Z)]]-, trifluoroacetate (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C23 H23 N7 O8 S4 . x C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

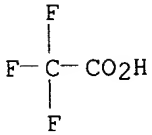
CRN 133897-69-5
CMF C23 H23 N7 O8 S4

Absolute stereochemistry.
Double bond geometry as shown.



CM 2

CRN 76-05-1
CMF C2 H F3 O2

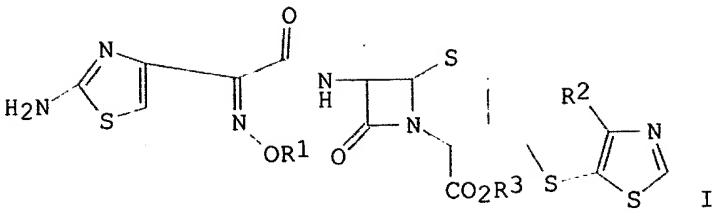


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 114:228629 Preparation of bis(thiazolyl) cephalosporins. Adam, Friedhelm; Duerckheimer, Walter; Scheunemann, Karl Heinz; Isert, Dieter; Seibert, Gerhard (Hoechst A.-G., Fed. Rep. Ger.). Eur. Pat. Appl. EP 409055 A1 19910123, 20 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (German). CODEN: EPXXDW. APPLICATION: EP 1990-113195 19900711. PRIORITY: DE 1989-3923541 19890715.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

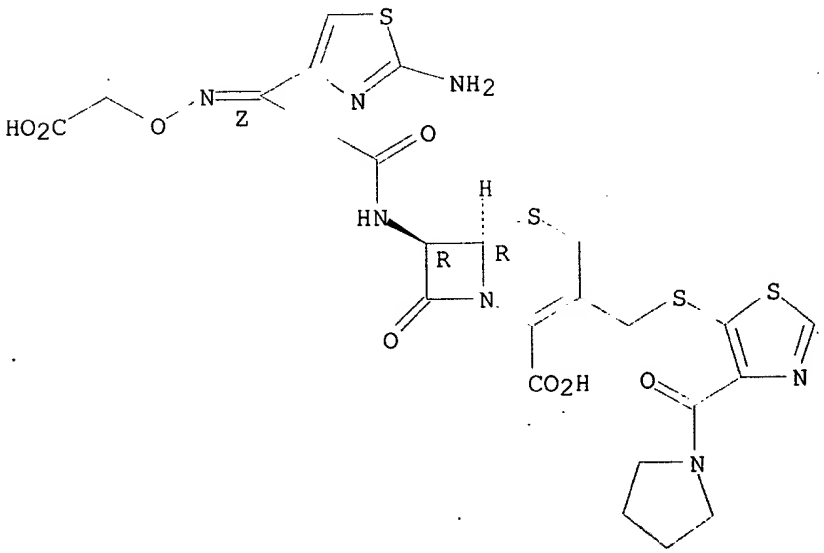


I

AB The title compds. [I; R1 = H, (substituted) alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkenyl, etc.; R2 = H, CO2H, alkoxycarbonyl, carbamoyl; R3 = H, cation, easily cleavable ester group], were prepd. as antibacgerials (no data). Thus, 2-aminothiazol-4-yl-2Z-methoxy = iminoacetic acid in DMF was treated with hydroxybenzotriazole and DCC; after 4 h, dicyclohexylurea was filtered off and 7-amin-3-[(4-methoxycarbonyl-1,3-thiazol-5-yl)thiomethyl]ceph-3-en-4-carboxylic acid (prepn. given) was added followed by stirring for 10 h to give 75% I (R 1 = Me, R2 = CO2Me, R3 = H).

L4 ANSWER 13 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 133897-69-5 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)[(carboxymethoxy)imino]acetyl]amino]-8-oxo-3-[[[4-(1-pyrrolidinylcarbonyl)-5-thiazolyl]thio]methyl]-, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C23 H23 N7 O8 S4
CI COM
SR CA

Absolute stereochemistry.
Double bond geometry as shown.

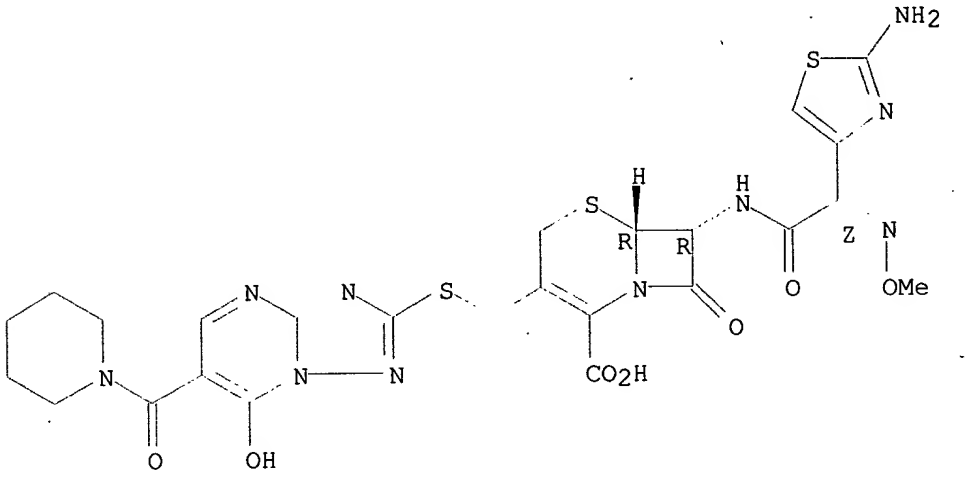


Searched by: Mary Hale 308-4258 CM-1 12D16

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L4 ANSWER 14 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 99951-83-4 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-3-[[[7-hydroxy-6-(1-piperidinylcarbonyl)[1,2,4]triazolo[1,5-a]pyrimidin-2-yl]thio]methyl]-8-oxo-, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN [1,2,4]Triazolo[1,5-a]pyrimidine, 5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid deriv.
FS STEREOSEARCH
MF C25 H26 N10 O7 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

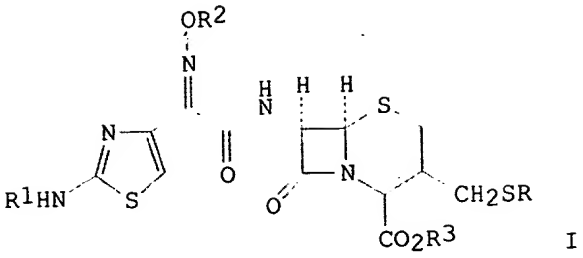
Absolute stereochemistry.
Double bond geometry as shown.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 104:68678 Cephalosporin derivatives and their use. Ohnishi, Haruo; Kosuzume, Hiroshi; Mizota, Masahiro; Suzuki, Yasuo; Mochida, Ei (Mochida Pharmaceutical Co., Ltd., Japan). Eur. Pat. Appl. EP 150507 A2 19850807, 222 pp. DESIGNATED STATES: R: AT, BE, CH, DE, FR, GB, IT, LI, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1984-116421 19841228. PRIORITY: JP 1983-247251 19831229; JP 1984-249193 19841126.
GI

Searched by: Mary Hale 308-4258 CM-1 12D16

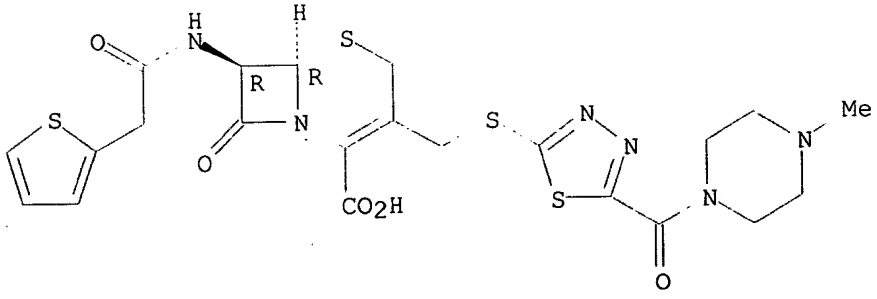


I

AB Cephalosporin derivs. I [R = heterocyclyl particularly triazolopyrimidyl or thiadiazolopyrimidyl; R1 = H or NH2-protecting group; R2 = H, Me, OH-protecting or acyl group; R3 = H, or carboxy-protecting group; wavy line represents an anti- or syn-form bond], which have strong antibacterial activity against gram-neg. and gram-pos. bacteria including methicillin-resistant Staphylococcus aureus, were prepd. Thus, 2-(2-chloroacetamido-4-thiazolyl)-2-[(Z)-methoxyimino]acetic acid was converted to the acid chloride and reacted with aminocephalosporanic acid to form (6R,7R)-3-acetoxymethyl-7-[2-(2-chloroacetamido-4-thiazolyl)-2-[(Z)-methoxyimino]acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (II). II was reacted with thiourea to form (6R,7R)-3-acetoxymethyl-7-[2-(2-amino-4-thiazolyl)-2-[(Z)-methoxyimino]acetamido]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid (III). 2-Carboxy-7-mercapto-5-methyl-s-triazolo[1,5-a]pyrimidine was reacted with III to form the cephalosporin deriv. (6R,7R)-7-[2-(2-amino-4-thiazolyl)-2-[(Z)-methoxyimino]acetamido]-3-[(2-carboxy-5-methyl-s-triazolo[1,5-a]pyrimidin-7-yl)thiomethyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-enecarboxylic acid (IV). The antibacterial activities and min. inhibitory concns. of 27 cephalosporins were detd. For example, IV had a min. inhibitory concn. against S. aureus of 1.57 .mu.g/mL.

L4 ANSWER 15 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 73332-02-2 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[5-[(4-methyl-1-piperazinyl)carbonyl]-1,3,4-thiadiazol-2-yl]thio]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C22 H24 N6 O5 S4
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.



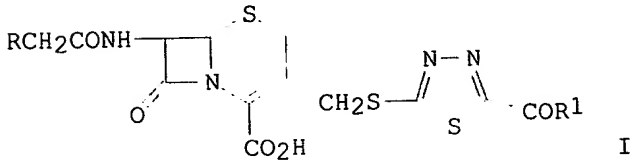
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 92:163979 Cephalosporin derivatives. Seki, Akio; Kai, Fumio; Saito, Toshinori; Kazuno, Yuzo; Miyauchi, Keinosuke; Ishii, Takahiro (Meiji Seika Kaisha, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 54128592 19791005 Showa, 10 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1978-36060 19780330.

GI



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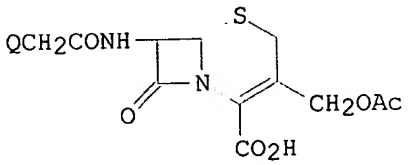

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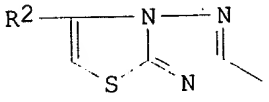
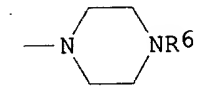
Q= 

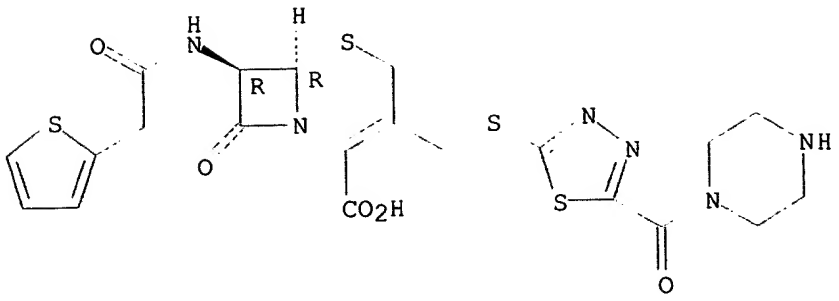
Q1= 

AB Seven cephalosporin derivs. I [R = 2-thienyl, Q (R2 = H, alkyl); R1 = R4R5N(CH2)nNR3 (R3, R4, R5 = H, alkyl; n = integers), Q1 (R6 = H, alkyl)] and II were prepd. by, e.g., N-acylation of 7-aminocephalosporanic acid (III) with QCH2CO2H (IV) or their CO2H reactive derivs. The bactericidal activities of I and II against Staphylococcus. aureus, Streptococcus faecalis, etc., were about 4 times as active as that of cefazolin. Thus, a mixt. of 3.5 g IV (R2 = Me) (V) and 7 g PCl5 in C6H6 was stirred 1 h at 20.degree. to give V chloride, which was mixed with 4.85 g III and 5.35 g Et3N in CH2Cl2 at -40.degree. and the mixt. stirred 30 min at room temp. to give, after treating with 0.5 N NaHCO3, 1.54 g II Na salt (R2 = Me).

L4 ANSWER 16 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 73332-01-1 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 8-oxo-3-[[[5-(1-piperazinylcarbonyl)-1,3,4-thiadiazol-2-yl]thio]methyl]-7-[(2-thienylacetyl)amino]-, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C21 H22 N6 O5 S4
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16

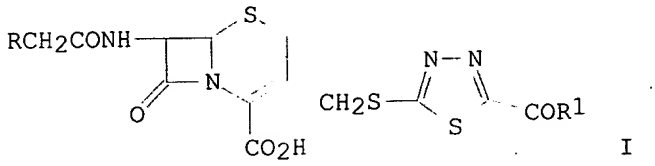


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 92:163979 Cephalosporin derivatives. Seki, Akio; Kai, Fumio; Saito, Toshinori; Kazuno, Yuzo; Miyauchi, Keinosuke; Ishii, Takahiro (Meiji Seika Kaisha, Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 54128592 19791005 Showa, 10 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1978-36060 19780330.

GI



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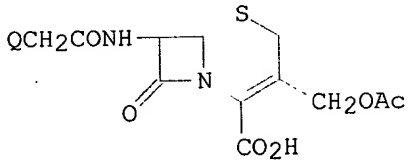
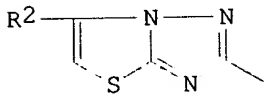
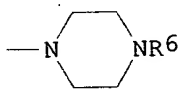


II

Q= 

Q1= 

AB Seven cephalosporin derivs. I [R = 2-thienyl, Q (R2 = H, alkyl); R1 = R4R5N(CH2)nNR3 (R3, R4, R5 = H, alkyl; n = integers), Q1 (R6 = H, alkyl)] and II were prepd. by, e.g., N-acylation of 7-aminocephalosporanic acid (III) with QCH2CO2H (IV) or their CO2H reactive derivs. The bactericidal activities of I and II against Staphylococcus. aureus, Streptococcus faecalis, etc., were about 4 times as active as that of cefazolin. Thus, a mixt. of 3.5 g IV (R2 = Me) (V) and 7 g PCl5 in C6H6 was stirred 1 h at 20.degree. to give V chloride, which was mixed with 4.85 g III and 5.35 g Et3N in CH2Cl2 at -40.degree. and the mixt. stirred 30 min at room temp. to give, after treating with 0.5 N NaHCO3, 1.54 g II Na salt (R2 = Me).

L4 ANSWER 17 OF 17 REGISTRY COPYRIGHT 2002 ACS
RN 66709-94-2 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid,

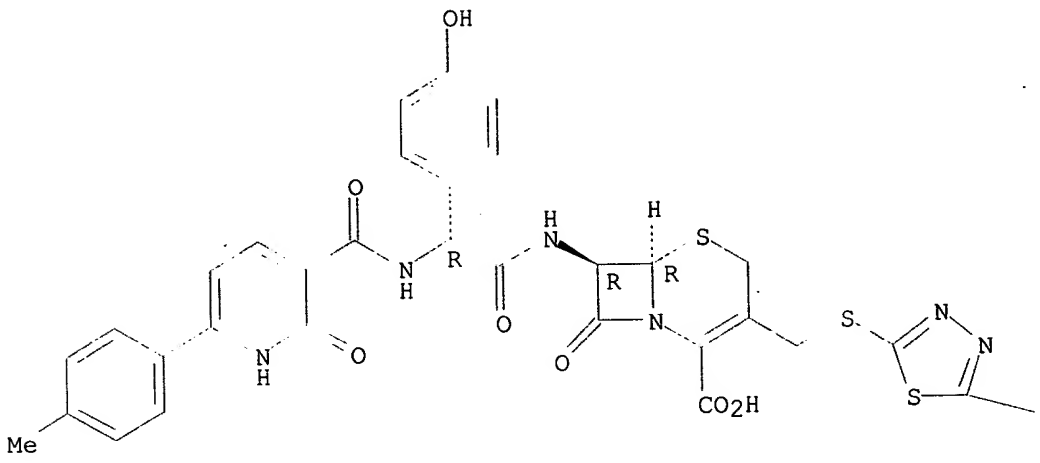
Searched by: Mary Hale 308-4258 CM-1 12D16

7-[[[[[1,2-dihydro-6-(4-methylphenyl)-2-oxo-3-pyridinyl]carbonyl]amino](4-hydroxyphenyl)acetyl]amino]-8-oxo-3-[[[5-(1-piperazinylcarbonyl)-1,3,4-thiadiazol-2-yl]thio]methyl]-, monosodium salt (9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C36 H34 N8 O8 S3 . Na
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

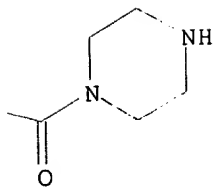
Absolute stereochemistry.

PAGE 1-A



● Na

PAGE 1-B

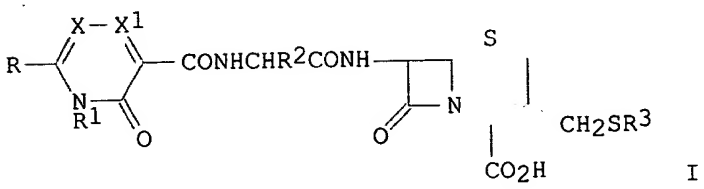


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 89:43459 Cephalosporin derivatives. Kai, Fumio; Tsuruoka, Takashi; Makabe, Osamu; Inouye, Shigeharu; Ikeda, Hitoshi; Kazuno, Yuzo; Nakajima, Shokichi; Seki, Shigeo; Niida, Taro (Meiji Seika Kaisha Ltd., Japan). Ger. Offen. DE 2744170 19780406, 100 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1977-2744170 19770930.

GI



I

AB Cephalosporins I (R = H, OH, alkyl, aryl, halogen, NH2, substituted amino, optionally substituted alkylthio, alkylsulfinyl, alkylsulfonyl, optionally substituted NHNH2, optionally substituted pyrazolo; R1 = H, alkyl, aryl; R2 = optionally substituted aryl, alkyl, cycloalkyl, cycloalkenyl, cycloalkadienyl, furyl, thienyl; R3 = optionally substituted thiadiazolyl, triazolyl, oxadiazolyl, tetrazolyl, triazinyl; X, X1 = N, CR4; R4 = H, halogen, OH, alkoxy, alkyl) were prepd. Thus, cephaloglycin was treated with p-nitrophenyl 2-hydroxy-6-(p-tolyl)-3-pyridinecarboxylate and 5-mercapto-1,3,4-thiadiazole-2-carboxamide to give I (X = X1 = CH, R = 4-MeC6H4, R1 = H, R2 = Ph, R3 = 5-carbanoyl-1,3,4-thiadiazol-2-yl), which had a min. inhibitory concn. against Staphylococcus aureus 209P JC-1 0.78 .mu.g/mL.

=> fil caol;s l4

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	206.12	206.27
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.44	-9.44

FILE 'CAOLD' ENTERED AT 09:16:25 ON 14 MAR 2002
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Searched by: Mary Hale 308-4258 CM-1 12D16

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.38	371.70

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-9.91

BERCIT
847525

FILE 'REGISTRY' ENTERED AT 08:10:40 ON 27 MAR 2002

STRUCTURE FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8
DICTIONARY FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS

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Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

=> d l5 que stat;d 1-3 ide cbib abs
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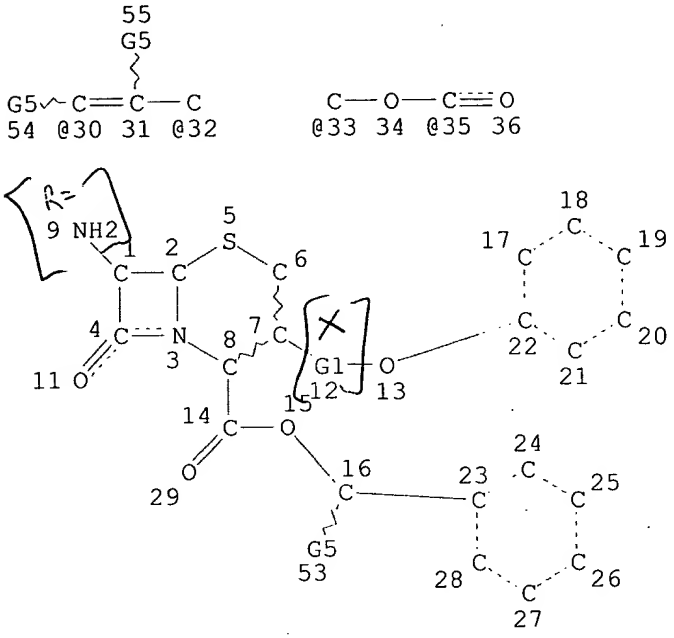

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DEFAULT ECLEVEL IS LIMITED

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NUMBER OF NODES IS 38

STEREO ATTRIBUTES: NONE
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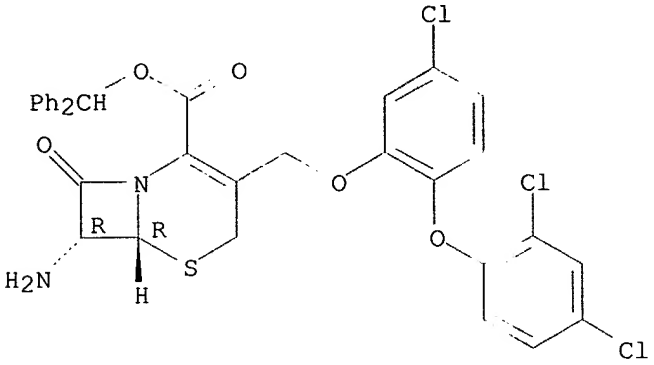
SEARCH TIME: 00.00.02

Searched by: Mary Hale 308-4258 CM-1 12D16

L5 ANSWER 1 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 371915-09-2 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-8-oxo-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H25 Cl3 N2 O5 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



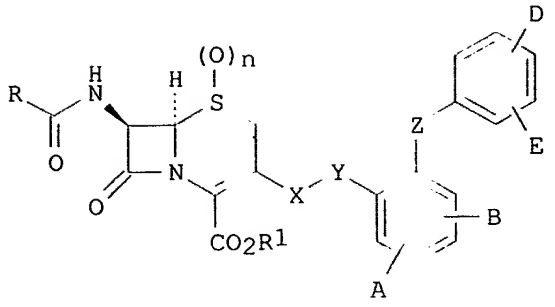
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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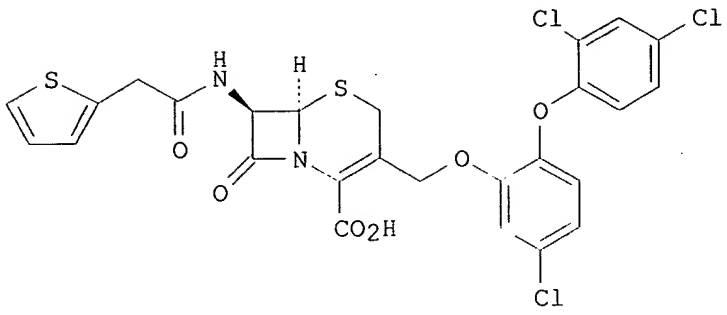


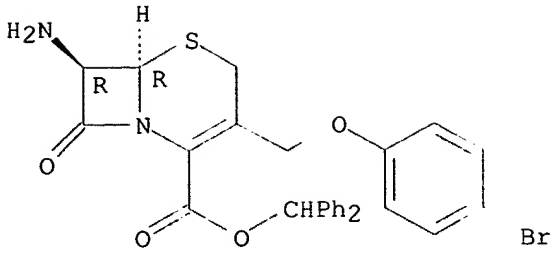
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L5 ANSWER 2 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 141874-22-8 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-3-[(4-bromophenoxy)methyl]-8-oxo-, diphenylmethyl ester, monohydrochloride, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H23 Br N2 O4 S . Cl H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 117:7704 Synthesis and antibacterial activities of new 3-phenoxymethylcephalosporins. Koyama, Kazuo; Saito, Shinichi; Kojima, Koichi (Med. Chem. Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan). J. Antibiot., 45(4), 535-41 (English) 1992. CODEN: JANTAJ. ISSN: 0021-8820.

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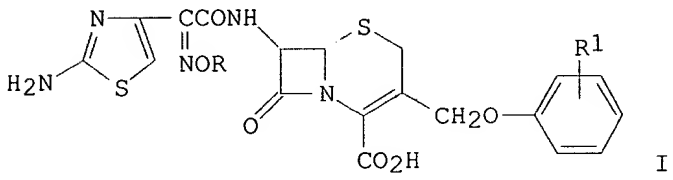


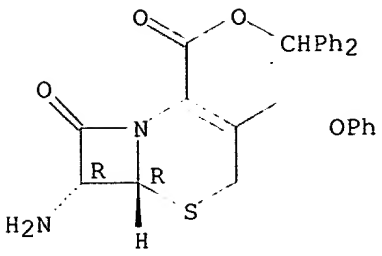
I

AB New 3-phenoxymethylcephalosporins I (R = H, R1 = H, F, Br, cyano, Ac, SMe, SOMe, CO2Me, CO2H, OMe; R = Me, CH2F, R1 = 3-F) were prepd. I exhibited good antibacterial activity against Gram-pos. and Gram-neg. bacteria.

L5 ANSWER 3 OF 3 REGISTRY COPYRIGHT 2002 ACS
RN 129543-64-2 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 7-amino-8-oxo-3-(phenoxymethyl)-, diphenylmethyl ester, monohydrochloride, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H24 N2 O4 S . Cl H
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



● HCl

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

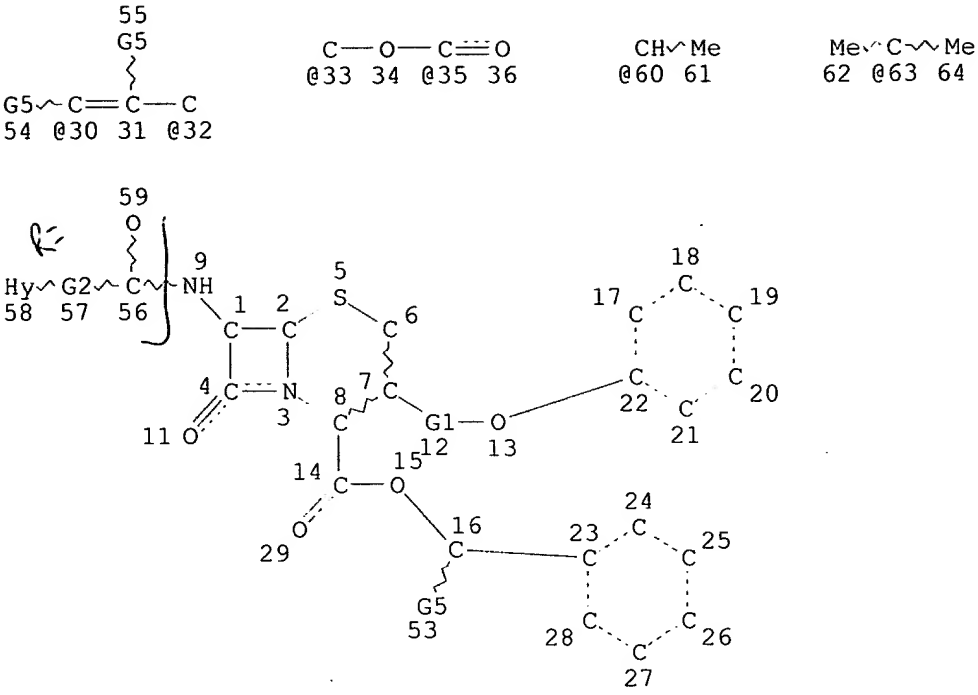
REFERENCE 1: 113:152140 3-Aryloxymethylcephalosporin derivatives as antibiotics and their preparation. Kojima, Koichi; Koyama, Kazuo; Amemiya, Shigeo; Iwata, Masayuki (Sankyo Co., Ltd., Japan). Eur. Pat. Appl. EP 363223 A2 19900411, 104 pp. DESIGNATED STATES: R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1989-310278 19891006. PRIORITY: JP 1988-253253 19881007.

GI For diagram(s), see printed CA Issue.

AB The title compds. I [R1 = H, acyl e.g., (substituted) C1-10 alkanoyl, C3-10 alkenoyl, etc.; R2 = H, C1-4 alkoxy; Ar = Ph with optional substituents such as C1-6 alkoxy, alkylthio, alkoxy, etc.; n = 0 or 1] were prepd. Diethylaniline, 2-(syn-trityloxyimino)-2-(2-tritylaminothiazol-4-yl)acetic acid, and POCl3 were added to diphenylmethyl 7-amino-3-phenoxymethyl-3-cephem-4-carboxylate hydrochloride in CH2Cl2. The reaction mixt. was stirred for 30 min to give a product, which was treated with HCO2H/MeOH and then deprotected in CF3CO2H/anisole to give title compd. syn-II.CF3CO2H. Compd. 7-[2-(2-aminothiazol-4-yl)-2-(syn-hydroxyimino)acetamido]-3-(4-carboxyphenoxy)methyl-3-cephem-4-carboxylic trifluoroacetate in vitro exhibited an MIC of 0.8 .mu.g/mL against Escherichia coli NIHJ(S).

=> d 18 que stat;d 1-14 ide cbib abs
L6 STR

Searched by: Mary Hale 308-4258 CM-1 12D16



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VAR G2=CH2/60/63
VAR G5=H/ME
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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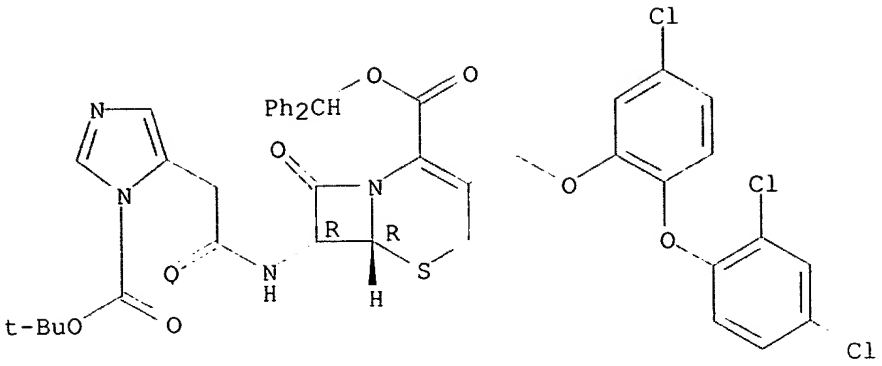
L8 ANSWER 1 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371915-12-7 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-7-[[[1-[(1,1-dimethylethoxy)carbonyl]-1H-imidazol-5-yl]acetyl]amino]-8-oxo-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C43 H37 Cl3 N4 O8 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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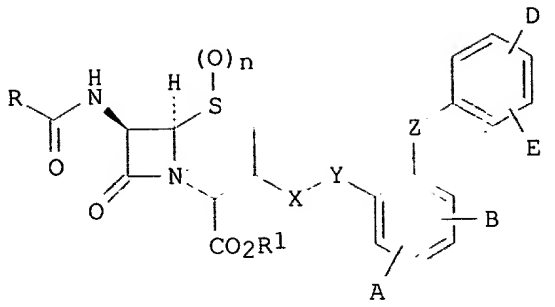
Searched by: Mary Hale 308-4258 CM-1 12D16



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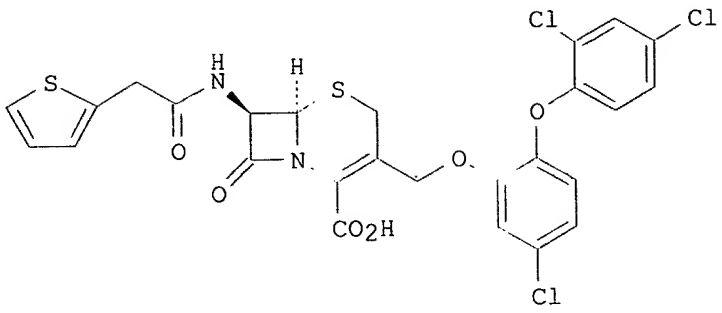


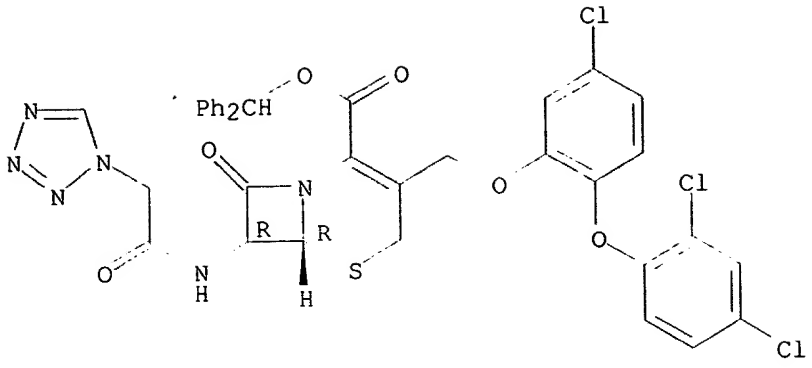
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 2 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371915-10-5 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-8-oxo-7-[(1H-tetrazol-1-ylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H27 Cl3 N6 O6 S
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



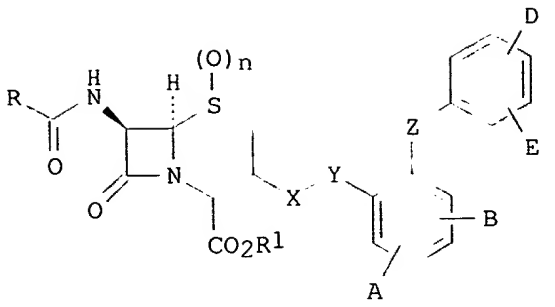
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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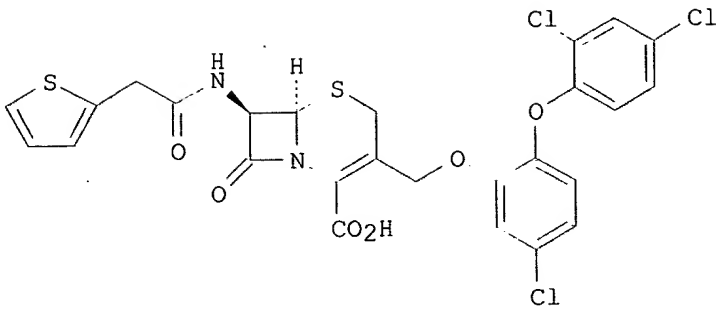


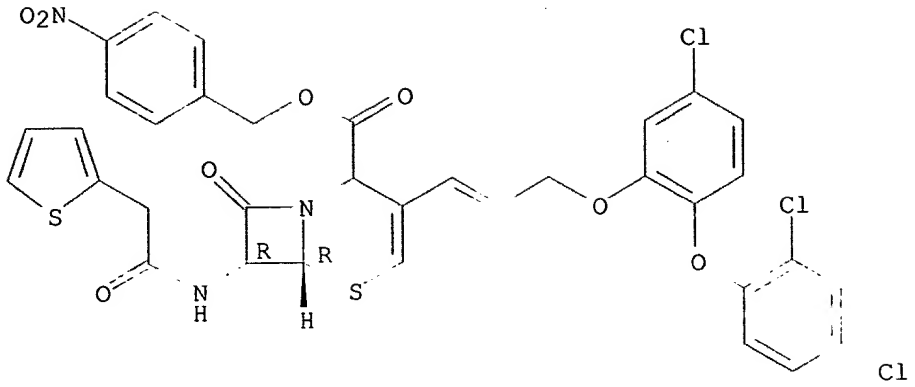
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 3 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371915-06-9 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid, 3-[3-[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]-1-propenyl]-8-oxo-7-[(2-thienylacetyl)amino]-, (4-nitrophenyl)methyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C35 H26 Cl3 N3 O8 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.
Double bond geometry unknown.

Searched by: Mary Hale 308-4258 CM-1 12D16



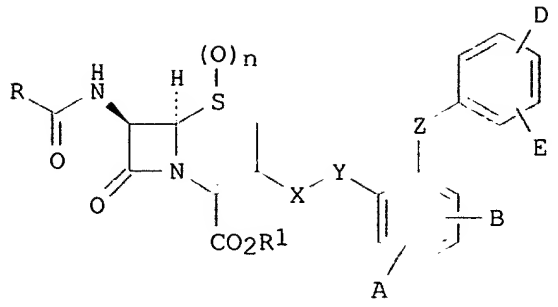
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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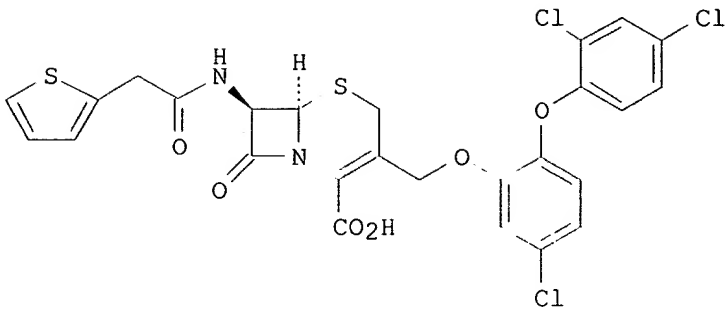


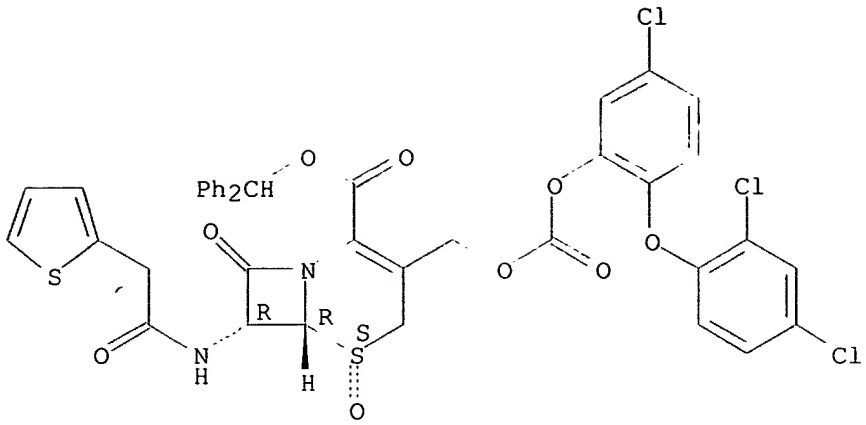
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 4 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371915-02-5 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, 5-oxide, (5S,6R,7R)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H29 Cl3 N2 O9 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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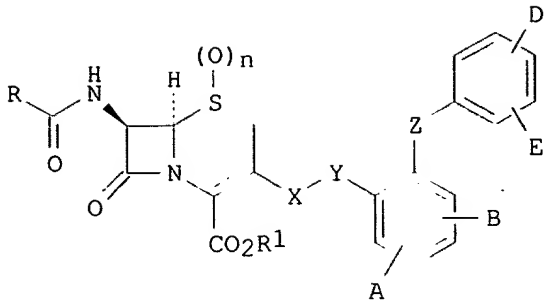
Searched by: Mary Hale 308-4258 CM-1 12D16



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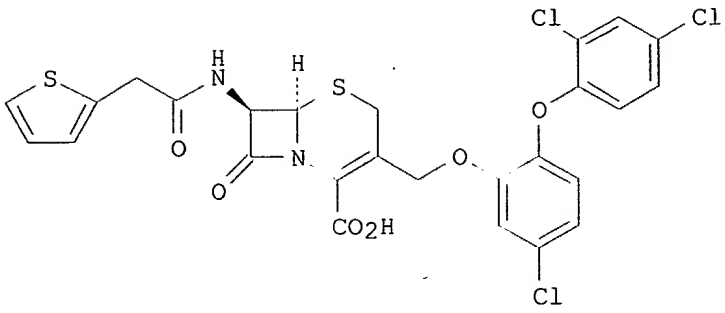


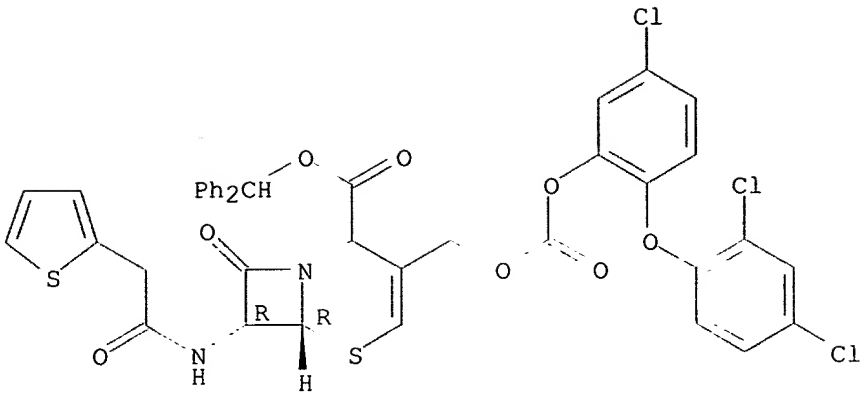
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 5 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371915-00-3 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid, 3-[[[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H29 Cl3 N2 O8 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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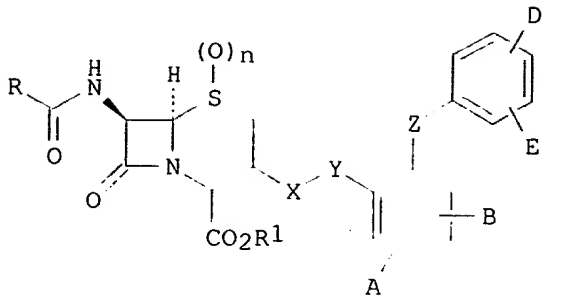
Searched by: Mary Hale 308-4258 CM-1 12D16



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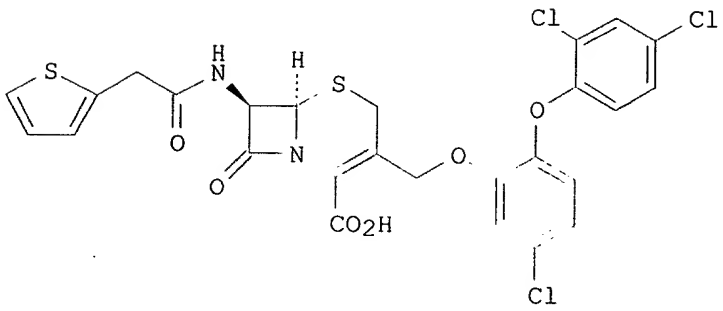


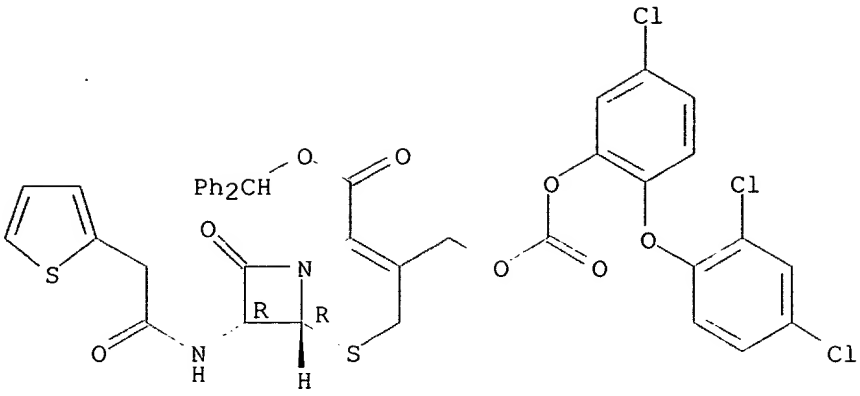
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 6 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371914-99-7 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C40 H29 Cl3 N2 O8 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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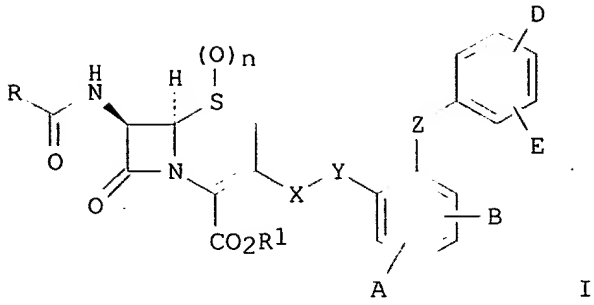
Searched by: Mary Hale 308-4258 CM-1 12D16



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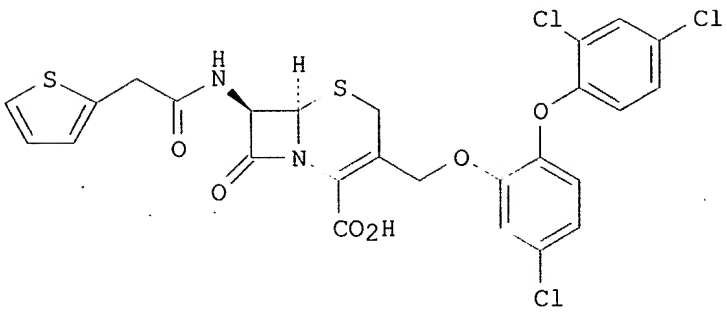


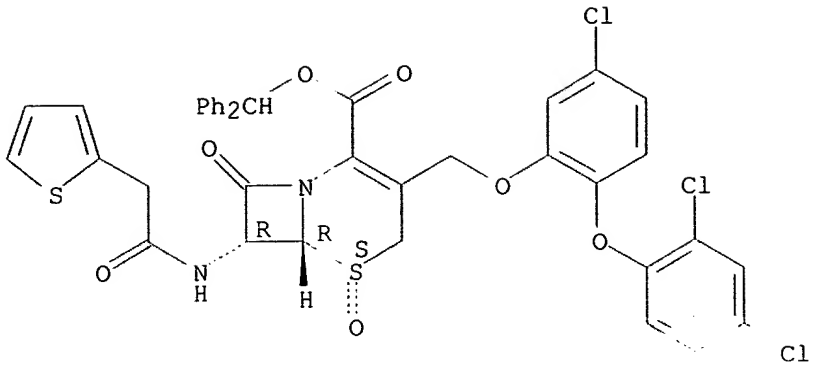
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 7 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371914-95-3 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, 5-oxide, (5S,6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H29 Cl3 N2 O7 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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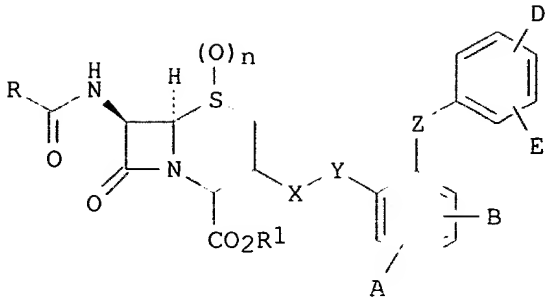
Searched by: Mary Hale 308-4258 CM-1 12D16



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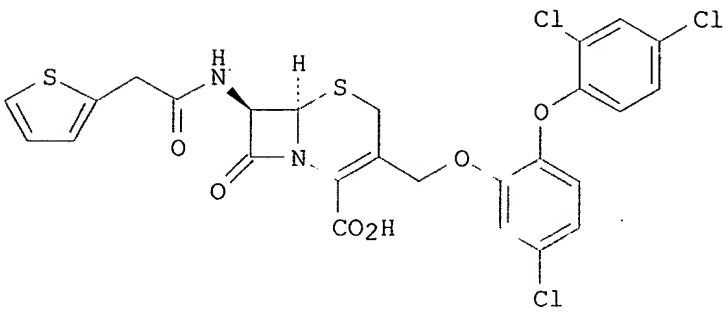


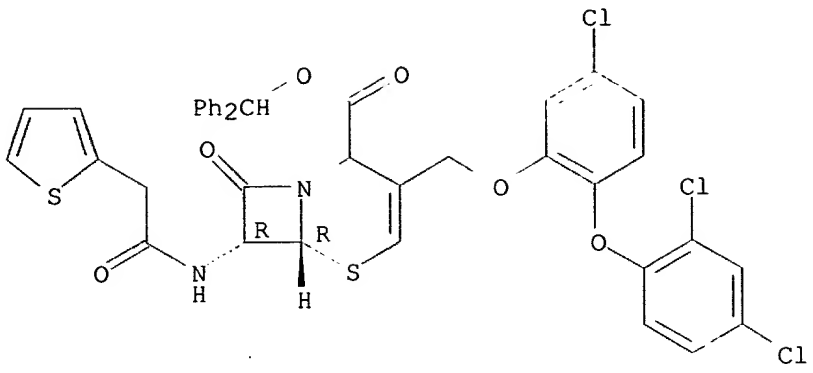
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 8 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371914-90-8 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid, 3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H29 Cl3 N2 O6 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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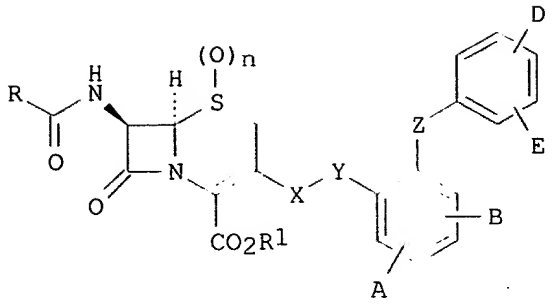
Searched by: Mary Hale 308-4258 CM-1 12D16



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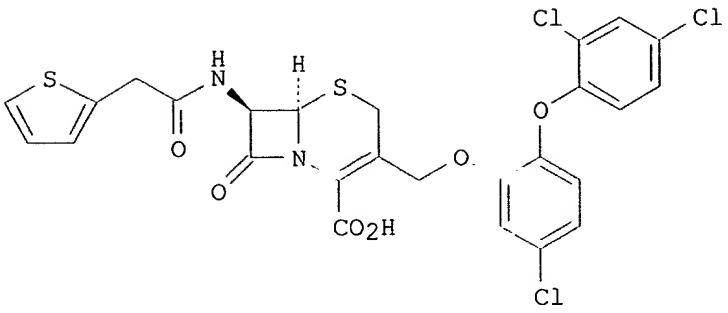


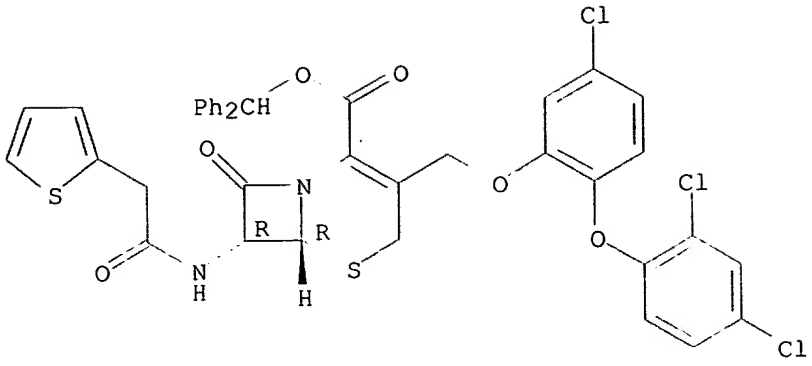
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 9 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 371914-89-5 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[5-chloro-2-(2,4-dichlorophenoxy)phenoxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C39 H29 Cl3 N2 O6 S2
SR CA
LC STN Files: CA, CAPLUS

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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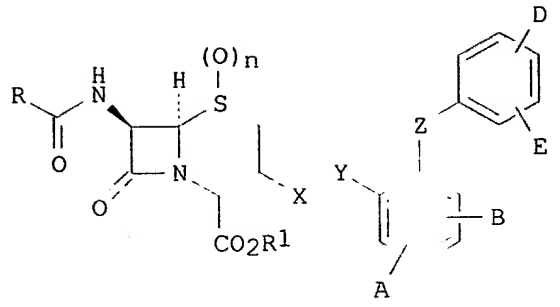
Searched by: Mary Hale 308-4258 CM-1 12D16



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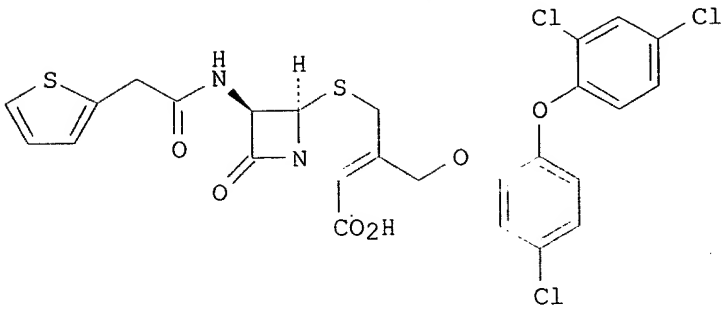


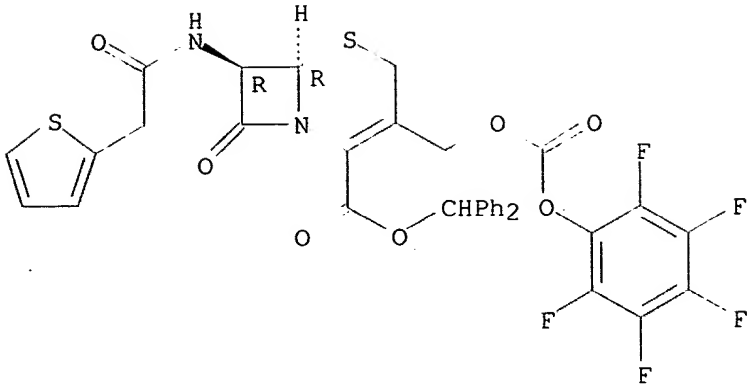
II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

L8 ANSWER 10 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 135508-69-9 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 8-oxo-3-[[[(pentafluorophenoxy)carbonyl]oxy]methyl]-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H23 F5 N2 O7 S2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:91903 Cephalosporin nitrogen mustard carbamate prodrugs for ADEPT. Alexander, Rikki P.; Beeley, Nigel R. A.; O'Driscoll, Maraid; O'Neill, Faye P.; Millican, T. Andrew; Pratt, Andrew J.; Willenbrock, Frances W. (CELLTECH, SLough/Berkshire, SL1 4EN, UK). Tetrahedron Lett., 32(27), 3269-72 (English) 1991. CODEN: TELEAY. ISSN: 0040-4039.

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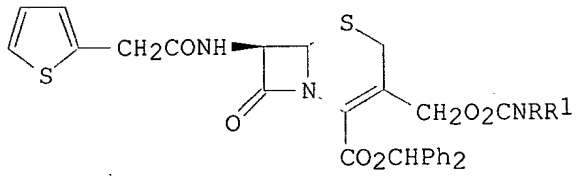


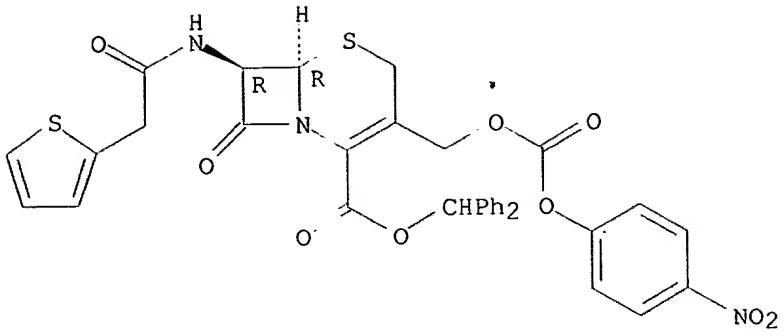
I

AB The carbamates I [R = R1 = CH2CH2Cl, CH2CH2Br, CH2CHMeCl, CH2CHMeBr; R = H, R1 = C6H4N(CH2CH2Cl)2-4] were prepd. from cephalothin. Hydrolysis of I by the .beta.-lactamase from Enterobacter cloacae P99 released the nitrogen mustard as well as cleaving the .beta.-lactam ring.

L8 ANSWER 11 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 135508-68-8 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R,7R)- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, (6R-trans)-
FS STEREOSEARCH
MF C34 H27 N3 O9 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:344322 Preparation of beta-lactams for inhibition of the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Chan, Ming Fai; Castillo, Rosario S.; Li, Qing; Doppalapudi, Venkata Ramana; Hixon, Mark Stephen; Lobl, Thomas J. (Newbiotics, Inc., USA). PCT Int. Appl. WO 2001083492 A1 20011108, 109 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US14133 20010501. PRIORITY: US 2000-PV201642 20000502.

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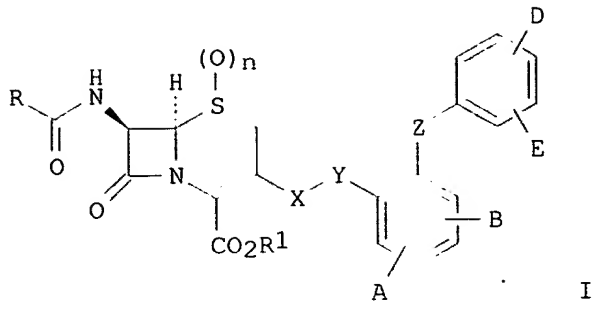
Searched by: Mary Hale 308-4258 CM-1 12D16



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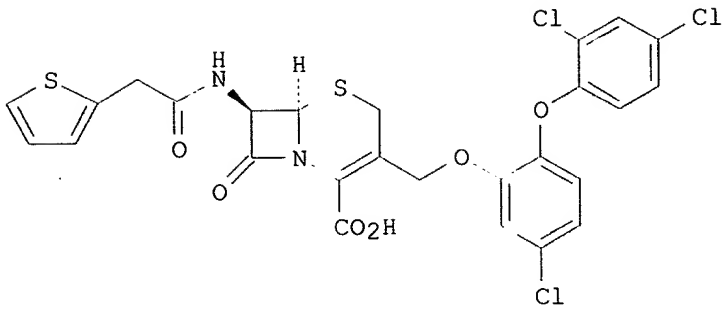

II

AB The present invention discloses the prepn. of beta-lactams [I; n = 0-2; A, B, D, E = same or different = halogen, H, CN, NO2, CF3, C(O)H, NH2, N(R2)n, OR2 (R2 = H, alkyl, alkenyl, alkynyl); X = CH2, cis-CH=CHCH2, trans-CH=CHCH2, CH2OC(O), NHC(O)O, PO3, SO3, SO2, traceless linker; Y = O, S, NR3; R3 = H, alkyl, alkenyl, alkynyl; Z = O, CO, S, .alpha.-NR4CO-.beta., .alpha.-N(R4)CO-.beta., N(R4)n (R4 = H, alkyl, alkenyl, alkynyl); wherein ring .alpha. connects Y to Z; Z = benzene or a heterocycle; ring .beta. connects to Z; R = Ph, PhCH2, PHOCH2, heterocycle, aryl, glycoside, etc; R1 = H, Li, Na, sugar, ammonium, NHMe, NMe2, alkylamine, polyethylene glycol], compns. and methods to inhibit the growth of both antibiotic sensitive and antibiotic resistant microorganisms. Thus, II was prepd. via a multistep synthetic sequence starting from 7-aminocephalosporanic acid, thiophene acetyl chloride, diphenyldiazomethane and triclosan. The prepd. beta-lactam derivs. were tested for bacterial growth inhibition properties [II showed IC50 = 42.4 nM vs E. coli N (.beta.-lactam sensitive strain) and IC50 = 21.0 nM vs E. coli C(Tem31-27) (.beta.-lactam resistant strain)].

REFERENCE 2: 123:198475 A practical synthetic method for 3-(N,N-disubstituted carbamoyloxy)methyl cephems without generating the .DELTA.2-isomers. Negi, Shigeto; Yamanaka, Motosuke; Komatsu, Yuki; Tsuruoka, Akihiko; Kamada, Atsushi; Tsukada, Itaru; Machida, Yoshimasa (Eisai Co., Ltd., Tsukuba Res. Labs., Ibaraki, 300-26, Japan). Chem. Pharm. Bull., 43(6), 1031-4 (English) 1995. CODEN: CPBTAL. ISSN: 0009-2363.

AB E1101, a new oral cephalosoprin, has a (N,N-dimethylcarbamoyloxy)methyl group at the C-3 position of the cephem nucleus. The previous methods for manufg. 3-(N,N-disubstituted carbamoyloxy)methyl cephems generated various amts. of intractable .DELTA.2 isomers as byproducts. In this report, we describe a new, practical synthetic method for cephems of this type without generating .DELTA.2 isomers, via 7-acylamino-3-(4-nitrophenoxy-carbonyloxy)methyl-.DELTA.3-cephem-4-carboxylic acid as a key

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intermediate.

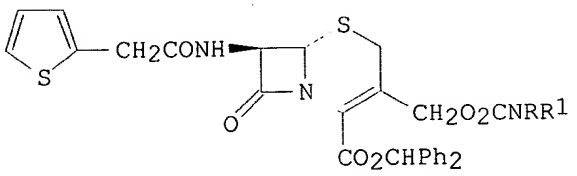
REFERENCE 3: 117:111379 Preparation of 7-acyl-3-(substituted carbamoyloxy)cephems as antibiotics. Negi, Shigeto; Yamanaka, Motosuke; Katsu, Kanemasa; Sugiyama, Isao; Komatu, Yuuki; Kamata, Atsushi; Tsuruoka, Akihiko; Machida, Yoshimasa (Eisai Co., Ltd., Japan). Eur. Pat. Appl. EP 484966 A2 19920513, 82 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-119065 19911108. PRIORITY: JP 1990-302783 19901109; JP 1991-40747 19910214; JP 1991-67709 19910308; JP 1991-169512 19910412.

GI For diagram(s), see printed CA Issue.

AB Title compds. [I; A = CH, N; R1 = (fluoro)alkoxy, (protected) OH; R2, R3 = alkyl, hydroxyalkyl, carbanoylalkyl, cyanoalkyl, or R2 = H, R3 = alkoxy, haloalkyl; NR2R3 = 4-6-membered heterocyclyl; R4 = (protected) carboxy], were prepd. Thus, Z-2-(2-tritylaminothiazol-4-yl)-2-trityloxyiminoacetic acid, 1-hydroxy-1H-benzotriazole, and DCC were stirred 30 min in DMF; benzylhydryl 7-amino-3-N,N-dimethylcarbamoyloxymethyl-3-cephem-4-carboxylate (prepn. given) was added and the mixt. was stirred 3 h to give 45% coupling product, which was treated with CF3CO2H/anisole and then HCO2H to give title compd. II. II showed a MIC of 0.2 .mu.g/mL against Staphylococcus aureus 209-P.

REFERENCE 4: 115:91903 Cephalosporin nitrogen mustard carbamate prodrugs for ADEPT. Alexander, Rikki P.; Beeley, Nigel R. A.; O'Driscoll, Maraid; O'Neill, Faye P.; Millican, T. Andrew; Pratt, Andrew J.; Willenbrock, Frances W. (CELLTECH, SLough/Berkshire, SL1 4EN, UK). Tetrahedron Lett., 32(27), 3269-72 (English) 1991. CODEN: TELEAY. ISSN: 0040-4039.

GI



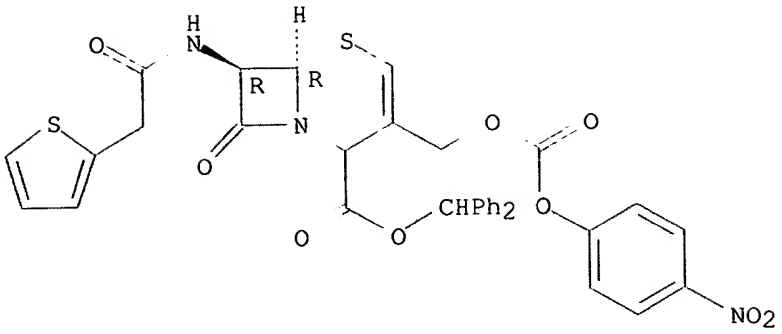
I

AB The carbamates I [R = R1 = CH2CH2Cl, CH2CH2Br, CH2CHMeCl, CH2CHMeBr; R = H, R1 = C6H4N(CH2CH2Cl)2-4] were prepd. from cephalothin. Hydrolysis of I by the .beta.-lactamase from Enterobacter cloacae P99 released the nitrogen mustard as well as cleaving the .beta.-lactam ring.

L8 ANSWER 12 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 134479-98-4 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-3-ene-2-carboxylic acid, 3-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, [6R-(6.alpha.,7.beta.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H27 N3 O9 S2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

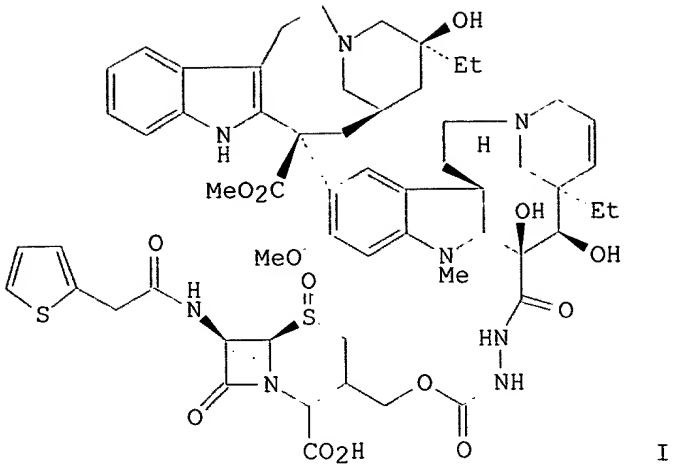
REFERENCE 1: 120:183013 Treatment of neoplastic diseases with antibody-enzyme conjugate and enzyme substrate-cytotoxic agent conjugate. Chen, Victor J.; Jungheim, Louis N.; Shepherd, Timothy A.; Meyer, Damon L. (Hybritech Inc., USA). PCT Int. Appl. WO 9401137 A1 19940120, 117 pp. DESIGNATED STATES: W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6324 19930702. PRIORITY: US 1992-909924 19920706.

AB Neoplastic diseases are treated by: (a) administering a therapeutically effective amt. of an antibody-enzyme conjugate to the affected host; and then (b) administering a therapeutically effective amt. of an enzyme substrate-cytotoxic agent conjugate to the affected host, wherein the substrate is a substrate for the enzyme. The substrate part of the conjugate compd. is a cephalosporin deriv. (Markush given) and the (antitumor) antibody is conjugated with .beta.-lactamase. Implanted colon tumors in mice were treated by administering .beta.-lactamase conjugated with a monoclonal antibody to carcinoembryonic antigen followed by administration of substrate-cytotoxic agent compd. 7-.beta.-(2-(thien-2-yl)acetamido)-3-(((desacetylvinblastinehydrazido)carbonyloxy)methylene)-3-cephem-1-.beta.-sulfoxide-4-carboxylic acid, trifluoroacetic acid salt (prepn. given).

REFERENCE 2: 116:194666 Synthesis of acylhydrazido-substituted cephems. Design of cephalosporin-vinca alkaloid prodrugs: substrates for an antibody targeted enzyme. Jungheim, Louis N.; Shepherd, Timothy A.; Meyer, Damon L. (Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA). J. Org. Chem., 57(8), 2334-40 (English) 1992. CODEN: JOCEAH. ISSN: 0022-3263.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



I

AB Cephalosporin substituted at the C-3' position with the potent oncolytic agent desacetylvinblastine hydrazide was synthesized as a potential prodrug for the treatment of solid tumors. The design of this novel prodrug was based on the knowledge that hydrolysis of a cephalosporin's .beta.-lactam bond can result in the expulsion of the C-3' substituent. Proper selection of the linkage used to join the cephem to the vinca, provided a releasable form of the drug as well as a chem. stable prodrug. We envisioned the conversion of prodrug to free vinca to be mediated by an immunoconjugate, consisting of a .beta.-lactamase enzyme covalently attached to a monoclonal antibody, which has been prelocalized at the tumor. Treatment of candidate prodrugs with the P99 .beta.-lactamase enzyme isolated from Enterobacter cloacae 265A efficiently catalyzed their conversion to the free drug form. A study of model compds. indicated that cephem 1-.beta.-sulfoxide was a better substrate for the enzyme than its sulfide counterpart. This finding prompted the synthesis of cephem sulfoxide I, which was efficiently accomplished via condensation of desacetylvinblastine hydrazide with the cephalothin derived cephem 3'-p-nitrophenyl carbonate.

REFERENCE 3: 115:49250 Cephalosporin-cytotoxic agent conjugates for delivering cytotoxic agents to tumor cells. (Lilly, Eli, and Co., USA; Hybritech, Inc.). Jpn. Kokai Tokkyo Koho JP 02247164 A2 19901002 Heisei, 45 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1990-23625 19900201. PRIORITY: US 1989-305824 19890202; US 1989-305900 19890202.

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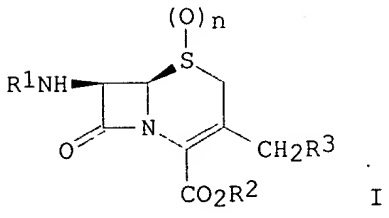


I

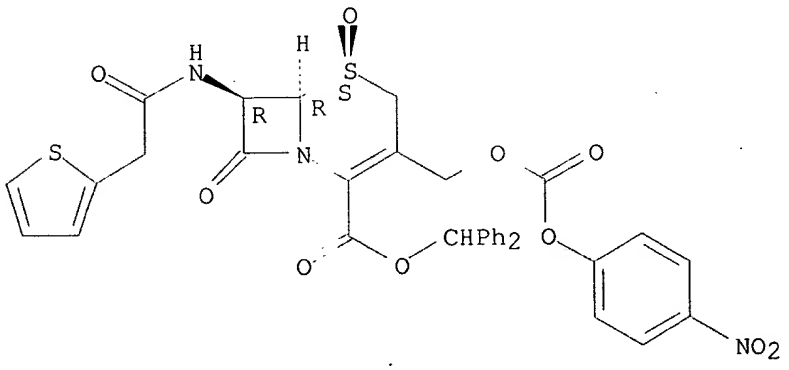
AB .beta.-D-Galactose-, D-amino acid peptide-, L-pyroglutamic acid-, or cephalosporin-cytotoxic agent conjugates [I; n = 0, 1; R1 = C1-30 alkyl-derived acyl; R2 = H, (in)org. cation, CO2H-protecting group,

Searched by: Mary Hale 308-4258 CM-1 12D16

metabolically unstable, nontoxic ester-forming group; R3 = cytotoxic ester-forming group; R3 = cytotoxic agent, e.g. desacetylvinblastine-aminoethanethiol, 5-fluorouracil, 7-(carboxyamino)desacetylcolchicine, N-(p-tosyl)-N'-(p-chlorophenyl)urea, N-[[(4-chlorophenyl)amino]carbonyl]-2,3-dihydro-1H-indene-5-sulfonamide, 1-demethoxydaunomycin and -adriamycin, methotrexate .gamma.-ester, etc.] which are cleaved by enzymes such as .beta.-lactamase, pyroglutamic acid aminopeptidase, .beta.-galactosidase, or D-aminopeptidase of the enzyme-antibody conjugates to release cytotoxic agents, are prepd. as antitumor agents. The enzyme-antibody conjugates using the antibodies to tumor antigens, e.g. cancer embryonal antigen, specifically bond to the malignant tumor cells and thereby a combination of the substrate-antitumor agent conjugate, 3.g. I, and the enzyme-antibody conjugates forms a kit for treatment of tumors and allows to release/deliver the antitumor agent to the tumor site at high concn. while reducing the side effect. Thus, deprotection of allyl 7-.beta.-[(2-thien-2-yl)acetamido]-3-[[1-(tert-butoxycarbonylamino)-2-ethylsulfido]methylene]-3-cephem-4-carboxylate with CF3CO2H/CH2Cl2 followed by condensation with desacetylvinblastine azide in the presence of N-methylmorpholine and removal of the allyl group with (Ph3P)4Pd, Et3Si, and Ph3P on EtOAc-hexane gave 7-.beta.-[2-(thien-2-yl)acetamido]-3-[[1-(desacetylvinblastine)amino]-2-ethylsulfido]methylene]-3-cephem-carboxylic acid (II). II in vitro inhibited 50% the intake of 3H-leucine in 75% leucine-deficient EBSS-MEN cells at 0.154 .mu.g/mL vs. 0.265 .mu.g/mL for a combination of II and .beta.-lactamase-antibody CEM231 conjugate and 0.26 .mu.g/mL for the cytotoxic agent desacetylvinblastine-aminoethanethiol.

L8 ANSWER 13 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 134479-96-2 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid, 3-[[[(4-nitrophenoxy)carbonyl]oxy]methyl]-8-oxo-7-[(2-thienylacetyl)amino]-, diphenylmethyl ester, 5-oxide, [5S-(5.alpha.,6.beta.,7.alpha.)]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C34 H27 N3 O10 S2
SR CA
LC STN Files: BEILSTEIN*, CA, CAPLUS, CASREACT, TOXCENTER
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

REFERENCE 1: 120:183013 Treatment of neoplastic diseases with antibody-enzyme conjugate and enzyme substrate-cytotoxic agent conjugate. Chen, Victor J.; Jungheim, Louis N.; Shepherd, Timothy A.; Meyer, Damon L. (Hybritech Inc., USA). PCT Int. Appl. WO 9401137 A1 19940120, 117 pp. DESIGNATED STATES: W: AU, BB, BG, BR, BY, CA, CZ, FI, HU, JP, KP, KR, KZ, LK, MG, MN, MW, NO, NZ, PL, RO, RU, SD, SK, UA, VN; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-US6324 19930702. PRIORITY: US 1992-909924 19920706.

AB Neoplastic diseases are treated by: (a) administering a therapeutically effective amt. of an antibody-enzyme conjugate to the affected host; and then (b) administering a therapeutically effective amt. of an enzyme substrate-cytotoxic agent conjugate to the affected host, wherein the substrate is a substrate for the enzyme. The substrate part of the conjugate compd. is a cephalosporin deriv. (Markush given) and the (antitumor) antibody is conjugated with .beta.-lactamase. Implanted colon tumors in mice were treated by administering .beta.-lactamase conjugated with a monoclonal antibody to carcinoembryonic antigen followed by administration of substrate-cytotoxic agent compd. 7-.beta.-(2-(thien-2-yl)acetamido)-3-(((desacetylvinblastinehydrazido)carbonyloxy)methylene)-3-cephem-1-.beta.-sulfoxide-4-carboxylic acid, trifluoroacetic acid salt (prepn. given).

REFERENCE 2: 119:95951 Synthesis of a cephalosporin-doxorubicin antitumor prodrug: a substrate for an antibody-targeted enzyme. Jungheim, Louis N.; Shepherd, Timothy A.; Kling, James K. (Lilly Res. Lab.; Eli Lilly and Co., Indianapolis, IN, 46285, USA). Heterocycles, 35(1), 339-48 (English) 1993. CODEN: HTCYAM. ISSN: 0385-5414.

GI

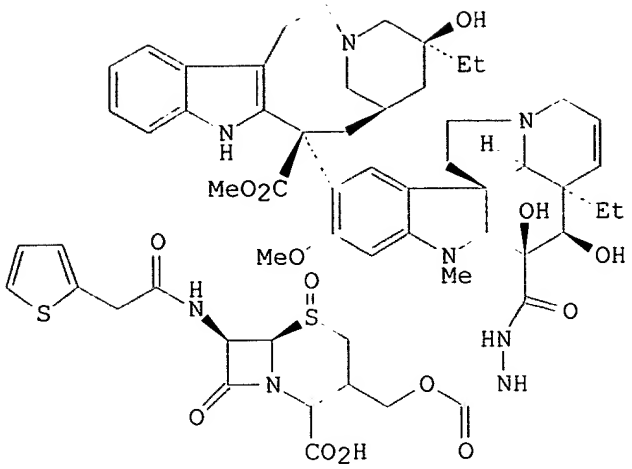
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Cephalosporin (I) substituted at the C-3' position with the potent oncolytic agent doxorubicin (II) was synthesized as a potential prodrug for the treatment of solid tumors. The conversion of prodrug to free doxorubicin to be mediated by an immunoconjugate, consisting of a .beta.-lactamase enzyme which is covalently attached to a monoclonal antibody, which has been prelocalized on the tumor cell surface was envisioned. Doxorubicin was covalently attached to the cephalosporin nucleus via a carbamate linkage. This was accomplished by condensation of the amino sugar moiety of doxorubicin with cephem 3'-p-nitrophenyl carbonate (III).

REFERENCE 3: 116:194666 Synthesis of acylhydrazido-substituted cephems. Design of cephalosporin-vinca alkaloid prodrugs: substrates for an antibody targeted enzyme. Jungheim, Louis N.; Shepherd, Timothy A.; Meyer, Damon L. (Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA). J. Org. Chem., 57(8), 2334-40 (English) 1992. CODEN: JOCEAH. ISSN: 0022-3263.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

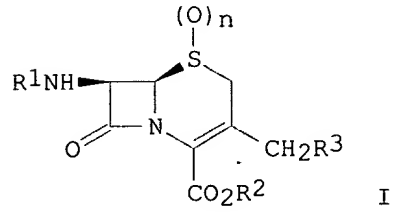


I

AB Cephalosporin substituted at the C-3' position with the potent oncolytic agent desacetylvinblastine hydrazide was synthesized as a potential prodrug for the treatment of solid tumors. The design of this novel prodrug was based on the knowledge that hydrolysis of a cephalosporin's .beta.-lactam bond can result in the expulsion of the C-3' substituent. Proper selection of the linkage used to join the cephem to the vinca, provided a releasable form of the drug as well as a chem. stable prodrug. We envisioned the conversion of prodrug to free vinca to be mediated by an immunoconjugate, consisting of a .beta.-lactamase enzyme covalently attached to a monoclonal antibody, which has been prelocalized at the tumor. Treatment of candidate prodrugs with the P99 .beta.-lactamase enzyme isolated from Enterobacter cloacae 265A efficiently catalyzed their conversion to the free drug form. A study of model compds. indicated that cephem 1-.beta.-sulfoxide was a better substrate for the enzyme than its sulfide counterpart. This finding prompted the synthesis of cephem sulfoxide I, which was efficiently accomplished via condensation of desacetylvinblastine hydrazide with the cephalothin derived cephem 3'-p-nitrophenyl carbonate.

REFERENCE 4: 115:49250 Cephalosporin-cytotoxic agent conjugates for delivering cytotoxic agents to tumor cells. (Lilly, Eli, and Co., USA; Hybritech, Inc.). Jpn. Kokai Tokkyo Koho JP 02247164 A2 19901002 Heisei, 45 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1990-23625 19900201. PRIORITY: US 1989-305824 19890202; US 1989-305900 19890202.

GI



I

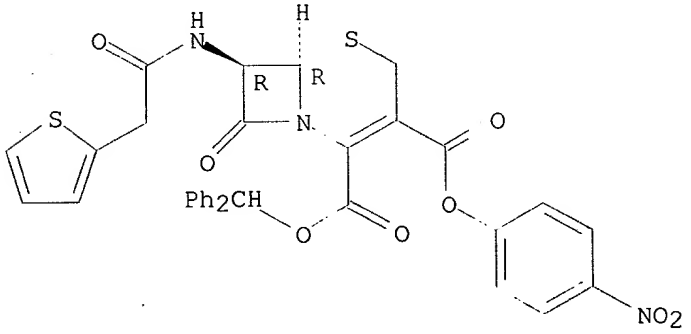
AB .beta.-D-Galactose-, D-amino acid peptide-, L-pyroglutamic acid-, or cephalosporin-cytotoxic agent conjugates [I; n = 0, 1; R1 = C1-30 alkyl-derived acyl; R2 = H, (in)org. cation, CO2H-protecting group,

Searched by: Mary Hale 308-4258 CM-1 12D16

metabolically unstable, nontoxic ester-forming group; R3 = cytotoxic ester-forming group; R3 = cytotoxic agent, e.g. desacetylvinblastine-aminoethanethiol, 5-fluorouracil, 7-(carboxyamino)desacetylcolchicine, N-(p-tosyl)-N'-(p-chlorophenyl)urea, N-[[(4-chlorophenyl)amino]carbonyl]-2,3-dihydro-1H-indene-5-sulfonamide, 1-demethoxydaunomycin and -adriamycin, methotrexate .gamma.-ester, etc.] which are cleaved by enzymes such as .beta.-lactamase, pyroglutamic acid aminopeptidase, .beta.-galactosidase, or D-aminopeptidase of the enzyme-antibody conjugates to release cytotoxic agents, are prepd. as antitumor agents. The enzyme-antibody conjugates using the antibodies to tumor antigens, e.g. cancer embryonal antigen, specifically bond to the malignant tumor cells and thereby a combination of the substrate-antitumor agent conjugate, 3.g. I, and the enzyme-antibody conjugates forms a kit for treatment of tumors and allows to release/deliver the antitumor agent to the tumor site at high concn. while reducing the side effect. Thus, deprotection of allyl 7-.beta.-[(2-thien-2-yl)acetamido]-3-[[1-(tert-butoxycarbonylamino)-2-ethylsulfido]methylene]-3-cephem-4-carboxylate with CF3CO2H/CH2Cl2 followed by condensation with desacetylvinblastine azide in the presence of N-methylmorpholine and removal of the allyl group with (Ph3P)4Pd, Et3Si, and Ph3P on EtOAc-hexane gave 7-.beta.-[2-(thien-2-yl)acetamido]-3-[[1-(desacetylvinblastine)amino]-2-ethylsulfido]methylene]-3-cephem-carboxylic acid (II). II in vitro inhibited 50% the intake of 3H-leucine in 75% leucine-deficient EBSS-MEN cells at 0.154 .mu.g/mL vs. 0.265 .mu.g/mL for a combination of II and .beta.-lactamase-antibody CEM231 conjugate and 0.26 .mu.g/mL for the cytotoxic agent desacetylvinblastine-aminoethanethiol.

L8 ANSWER 14 OF 14 REGISTRY COPYRIGHT 2002 ACS
RN 55243-84-0 REGISTRY
CN 5-Thia-1-azabicyclo[4.2.0]oct-2-ene-2,3-dicarboxylic acid, 8-oxo-7-[(2-thienylacetyl)amino]-, 2-(diphenylmethyl) 3-(4-nitrophenyl) ester, (6R-trans)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C33 H25 N3 O8 S2
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 82:170811 3-Carboxycephem. Spry, Douglas O. (Lilly Res. Labs., Eli Lilly Co., Indianapolis, Indiana, USA). J. Chem. Soc., Chem. Commun. (24), 1012-13 (English) 1974. CODEN: JCCCAT.
GI For diagram(s), see printed CA Issue.

Searched by: Mary Hale 308-4258 CM-1 12D16

AB The diacid I was prepd. from the ethylene acetal II in 6 steps. I was converted into 3-ketones, amides, and N-cephem acylamines.

=> fil caol;s l8

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	356.64	728.34

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-10.03	-19.94

FILE 'CAOLD' ENTERED AT 08:30:59 ON 27 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

L9 0 L8

=> fil reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.38	728.72

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-19.94

FILE 'REGISTRY' ENTERED AT 08:31:03 ON 27 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8
DICTIONARY FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

Searched by: Mary Hale 308-4258 CM-1 12D16

http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

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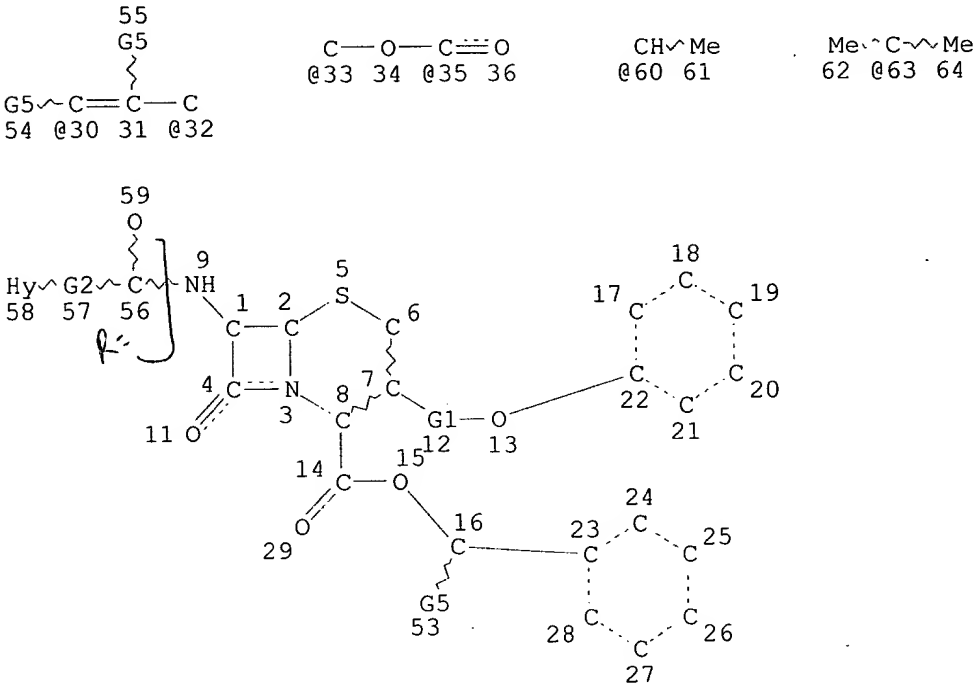


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DEFAULT ECLEVEL IS LIMITED

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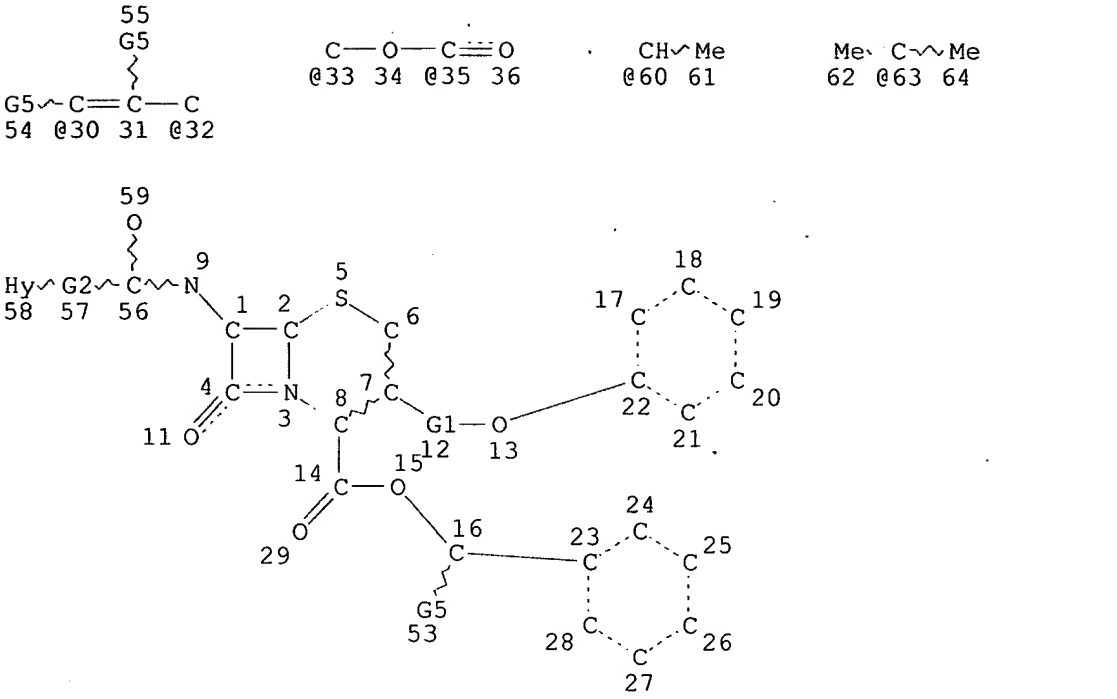
Searched by: Mary Hale 308-4258 CM-1 12D16



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VAR G2=CH2/60/63
VAR G5=H/ME
NODE ATTRIBUTES:
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 47

STEREO ATTRIBUTES: NONE
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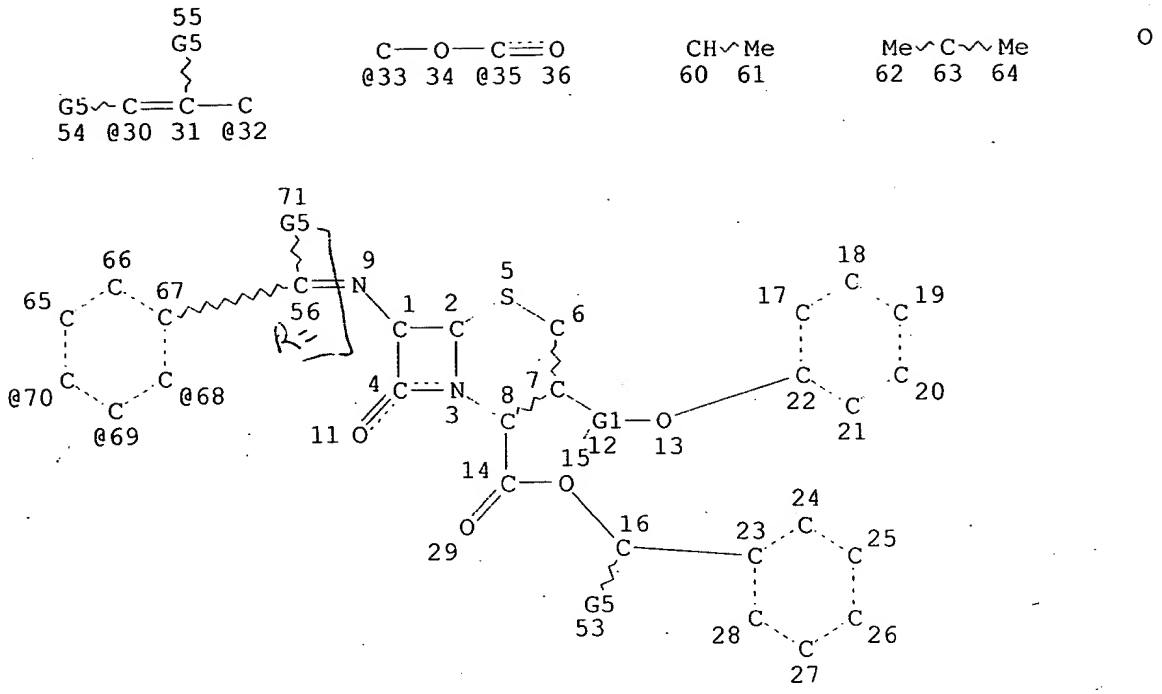
Searched by: Mary Hale 308-4258 CM-1 12D16



Page 1-A

H @72

Page 1-B
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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	282.08	1010.80
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-19.94

Searched by: Mary Hale 308-4258 CM-1 12D16

BIRCH
847525

FILE 'REGISTRY' ENTERED AT 08:34:26 ON 27 MAR 2002
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8
DICTIONARY FILE UPDATES: 25 MAR 2002 HIGHEST RN 402820-22-8

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

The P indicator for Preparations was not generated for all of the CAS Registry Numbers that were added to the H/Z/CA/CAplus files between 12/27/01 and 1/23/02. Use of the P indicator in online and SDI searches during this period, either directly appended to a CAS Registry Number or by qualifying an L-number with /P, may have yielded incomplete results. As of 1/23/02, the situation has been resolved. Also, note that searches conducted using the PREP role indicator were not affected.

Customers running searches and/or SDIs in the H/Z/CA/CAplus files incorporating CAS Registry Numbers with the P indicator between 12/27/01 and 1/23/02, are encouraged to re-run these strategies. Contact the CAS Help Desk at 1-800-848-6533 in North America or 1-614-447-3698, worldwide, or send an e-mail to help@cas.org for further assistance or to receive a credit for any duplicate searches.

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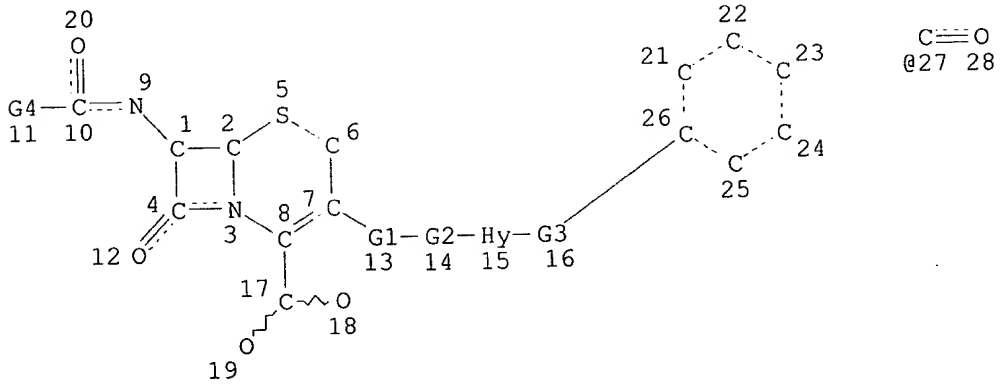

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VAR G4=H/C

Searched by: Mary Hale 308-4258 CM-1 12D16

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GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 34

STEREO ATTRIBUTES: NONE
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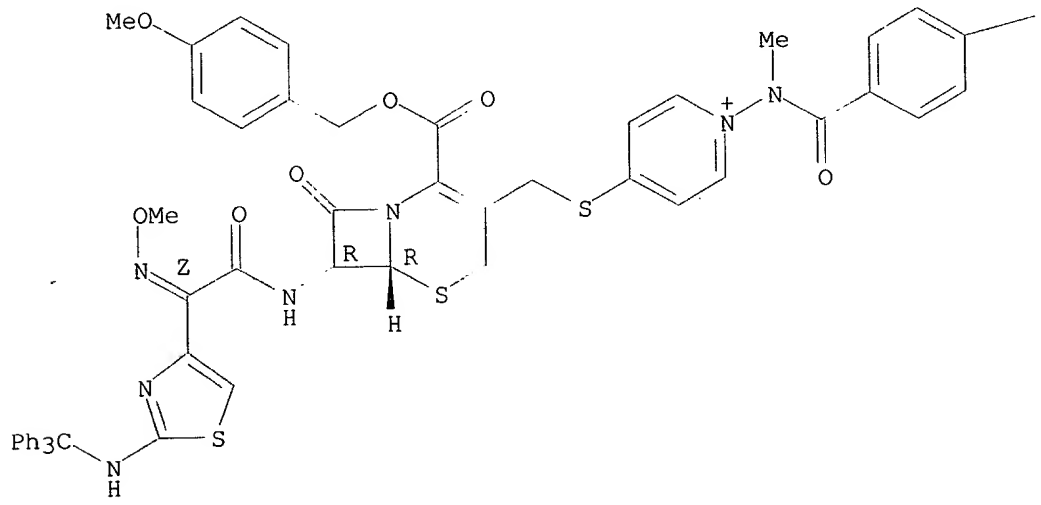
SEARCH TIME: 00.00.10

L3 ANSWER 1 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 153136-71-1 REGISTRY
CN Pyridinium, 1-[(4-carboxybenzoyl)methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, monosodium salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C55 H48 N7 O9 S3 . I . Na
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



● Na

Searched by: Mary Hale 308-4258 CM-1 12D16

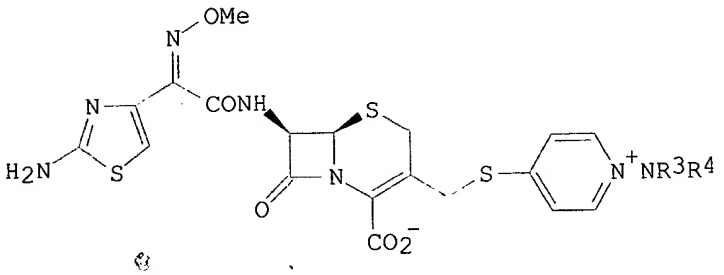
—CO_2H

● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

GI



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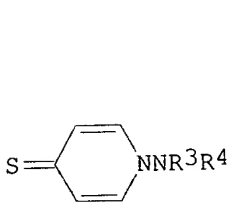

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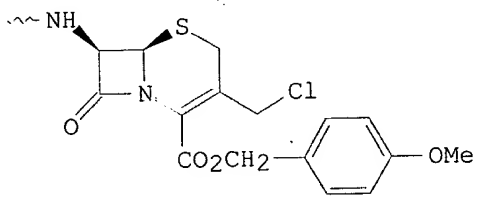


III

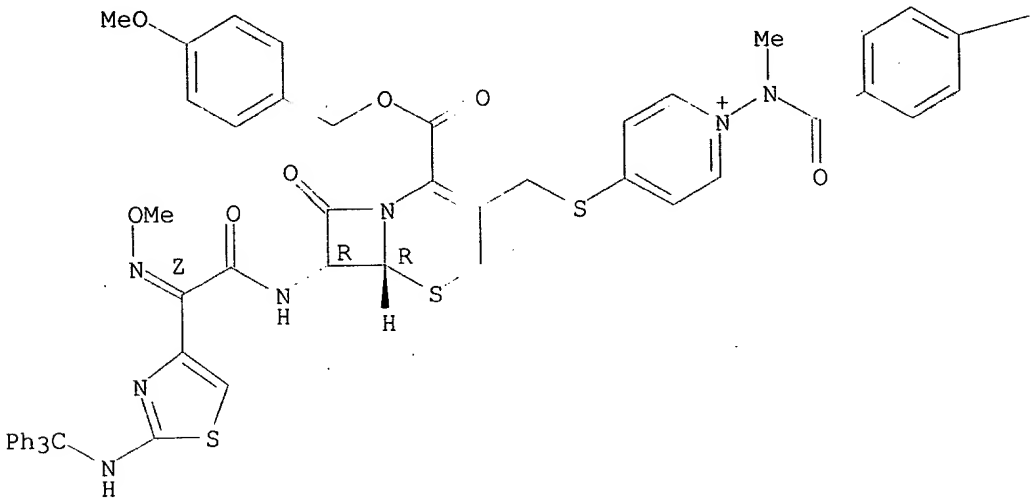
AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

Searched by: Mary Hale 308-4258 CM-1 12D16

L3 ANSWER 2 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 153136-70-0 REGISTRY
CN Pyridinium, 1-[(4-aminobenzoyl)methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C54 H49 N8 O7 S3 . I
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

—NH2

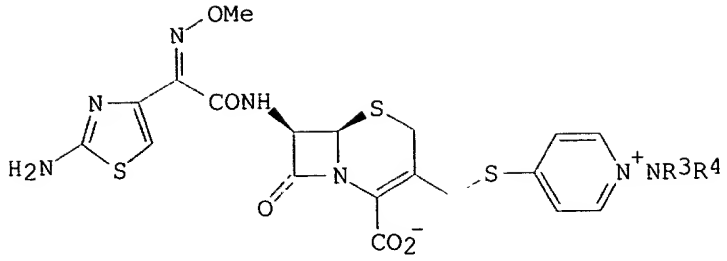
● I⁻

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

Searched by: Mary Hale 308-4258 CM-1 12D16

GI



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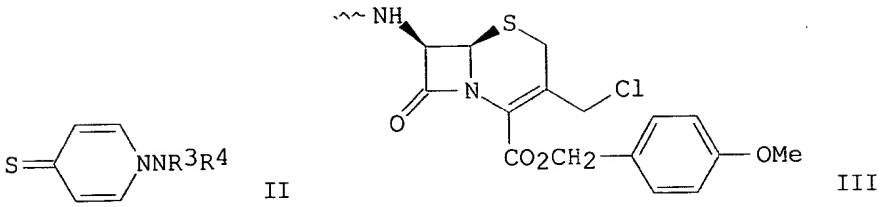


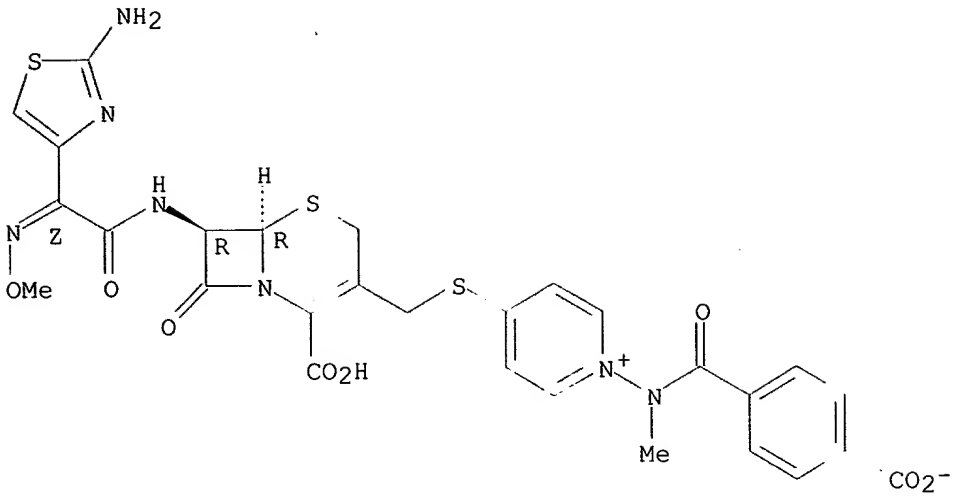
II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

L3 ANSWER 3 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134947-40-3 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(4-carboxybenzoyl)methylamino]-, inner salt, monosodium salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
DR 153136-74-4
MF C28 H25 N7 O8 S3 . Na
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

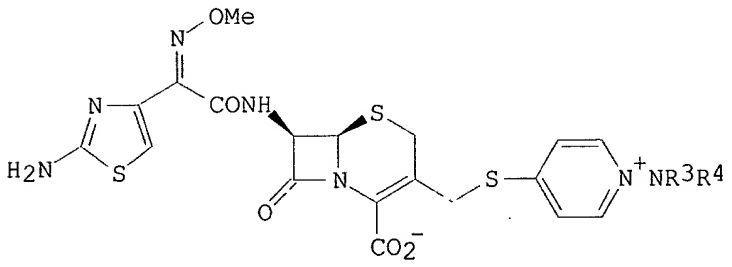


● Na

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

GI



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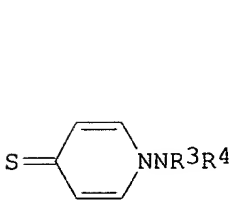

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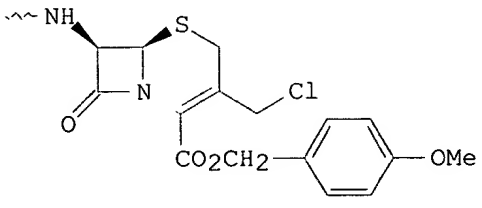


III

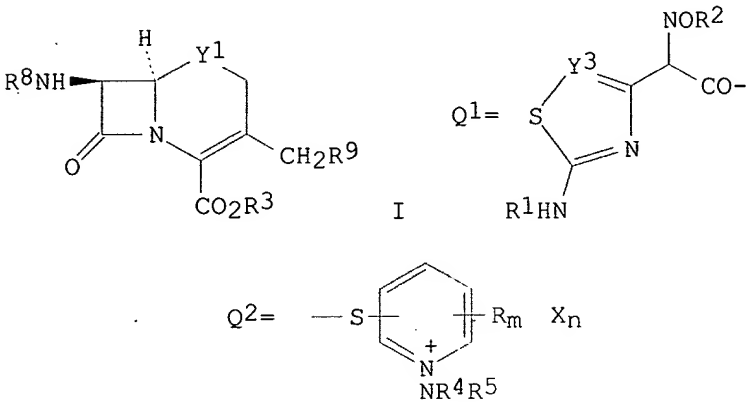
AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-

Searched by: Mary Hale 308-4258 CM-1 12D16

(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

REFERENCE 2: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

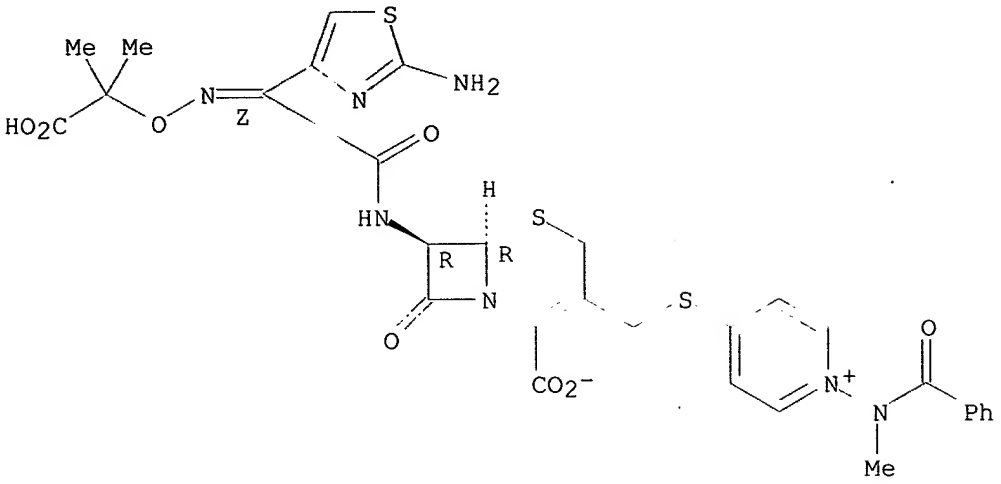


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 4 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134947-39-0 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(benzoylmethylamino)-, inner salt, monosodium salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H29 N7 O8 S3 . Na
SR CA
LC STN Files: CA, CAPLUS, USPATFULL
CRN (134481-71-3)

Searched by: Mary Hale 308-4258 CM-1 12D16

Absolute stereochemistry.
Double bond geometry as shown.

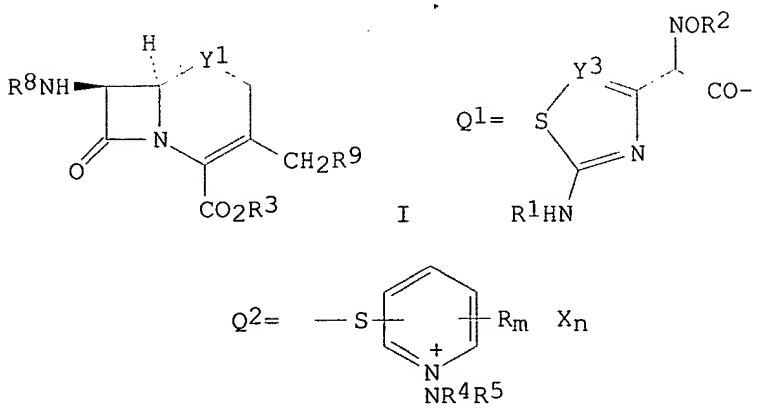


● Na

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl,

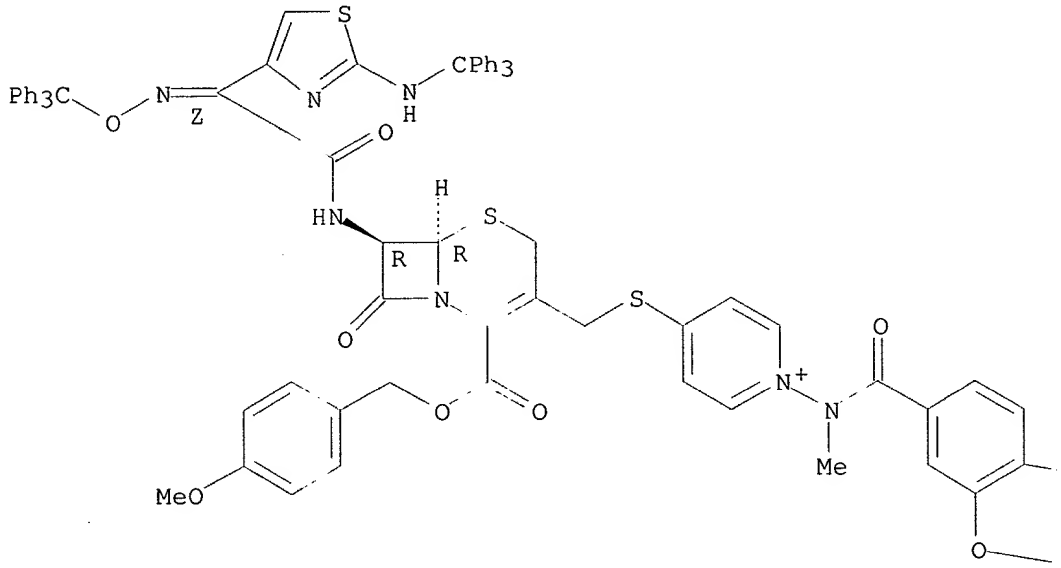
Searched by: Mary Hale 308-4258 CM-1 12D16

aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

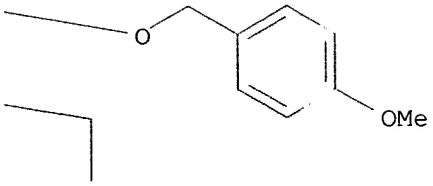
L3 ANSWER 5 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134510-25-1 REGISTRY
CN Pyridinium, 1-[[3,4-bis[(4-methoxyphenyl)methoxy]benzoyl]methylamino]-4-[[[2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-7-[[[(triphenylmethoxy)imino][2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C88 H76 N7 O11 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



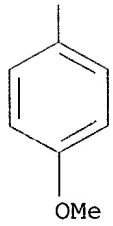
PAGE 1-B



PAGE 2-A

● I^-

PAGE 2-B



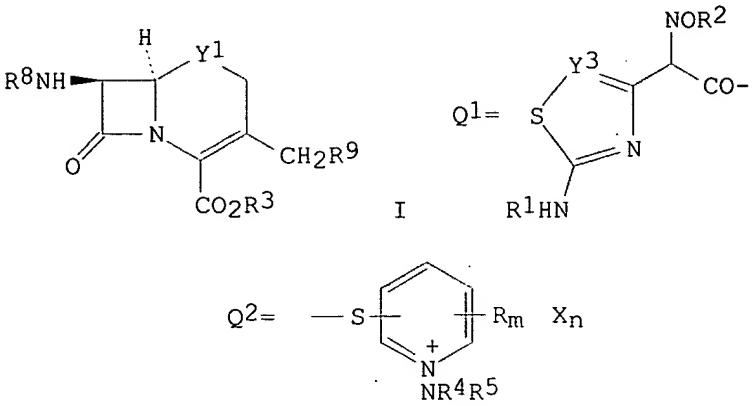
1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxy

Searched by: Mary Hale 308-4258 CM-1 12D16

lates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



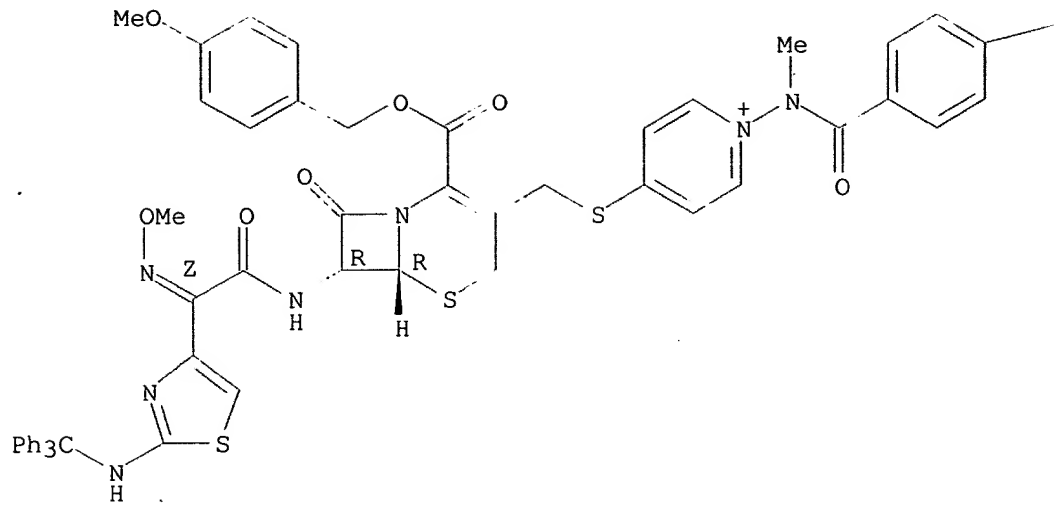
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 6 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-75-0 REGISTRY
CN Pyridinium, 1-[[4-[[(1,1-dimethylethoxy)carbonyl]amino]benzoyl]methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C59 H57 N8 O9 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



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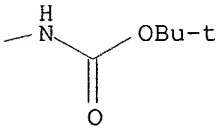

● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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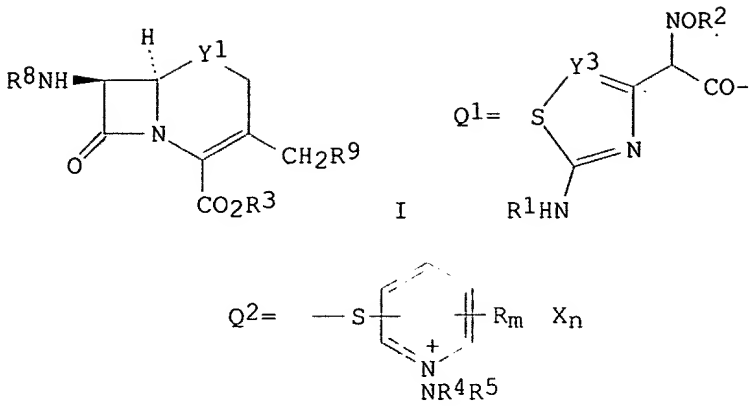
Searched by: Mary Hale 308-4258 CM-1 12D16



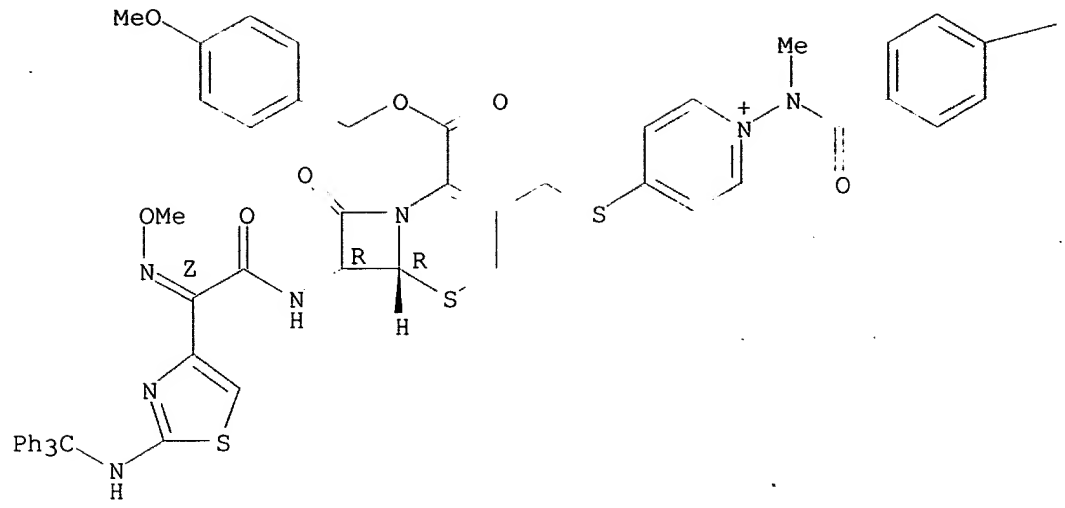
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 7 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-74-9 REGISTRY
CN Pyridinium, 1-[[4-[(diphenylmethoxy)carbonyl]benzoyl]methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C68 H58 N7 O9 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

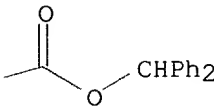
Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



PAGE 1-B



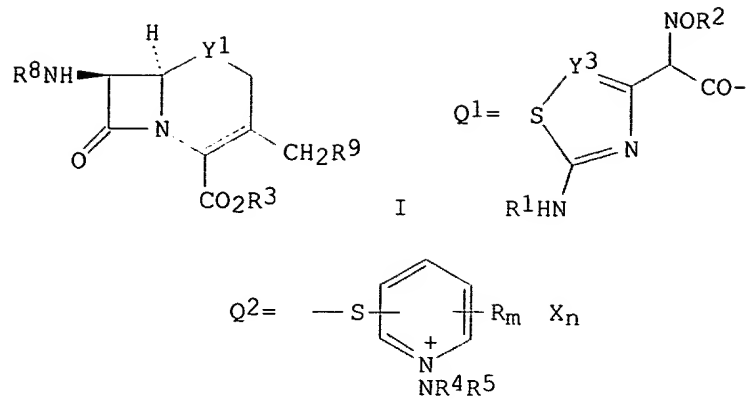
● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



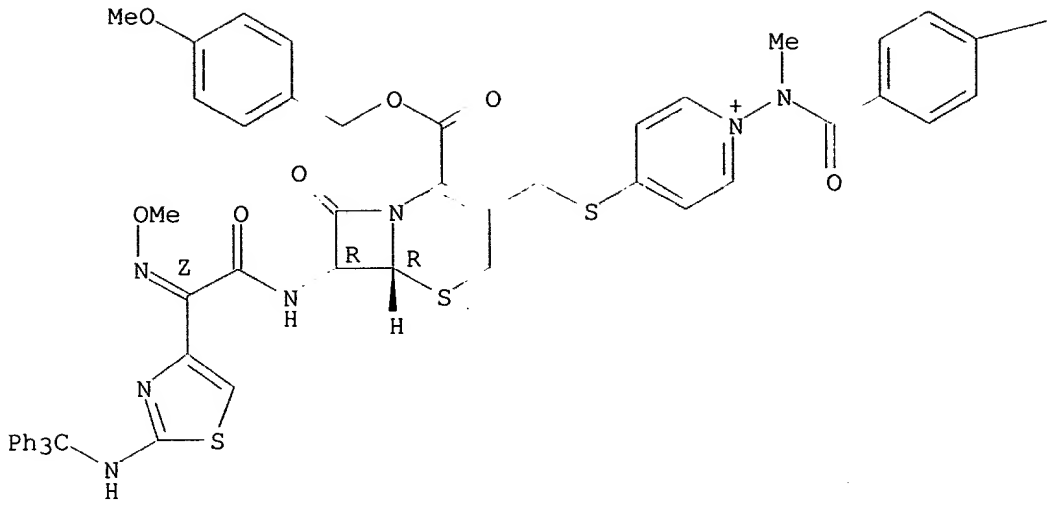
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 8 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-68-1 REGISTRY
CN Pyridinium, 1-[(4-methoxybenzoyl)methylamino]-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C55 H50 N7 O8 S3 . I
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



PAGE 1-B

OMe

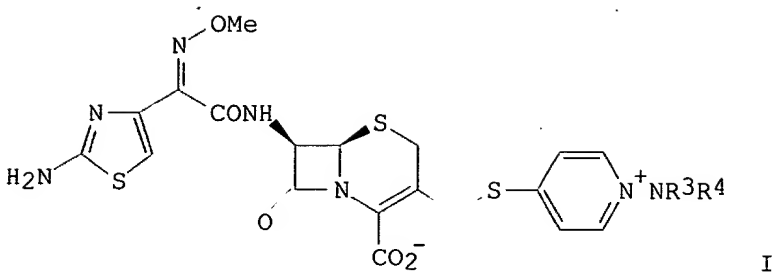
● I^-

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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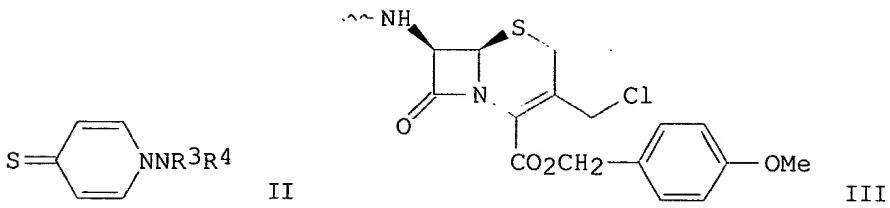
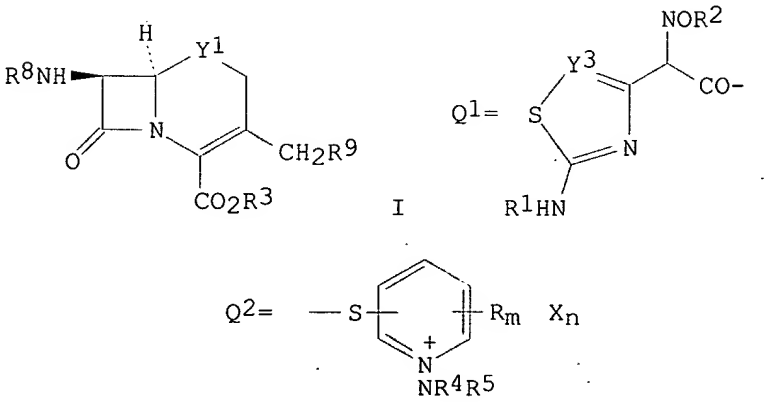


II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

REFERENCE 2: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



I

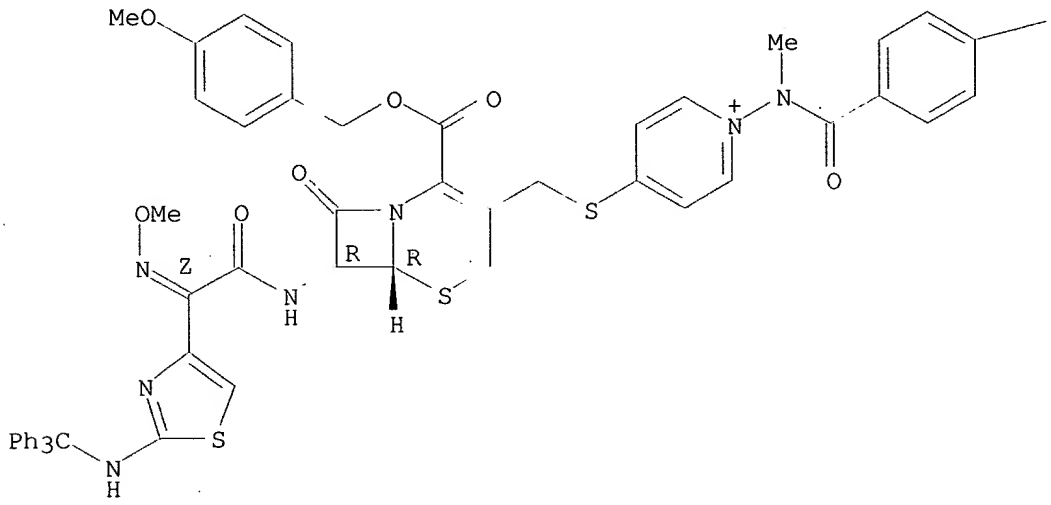
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 =

thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2. = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 9 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-67-0 REGISTRY
CN Pyridinium, 4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[methyl(4-nitrobenzoyl)amino]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C54 H47 N8 O9 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B

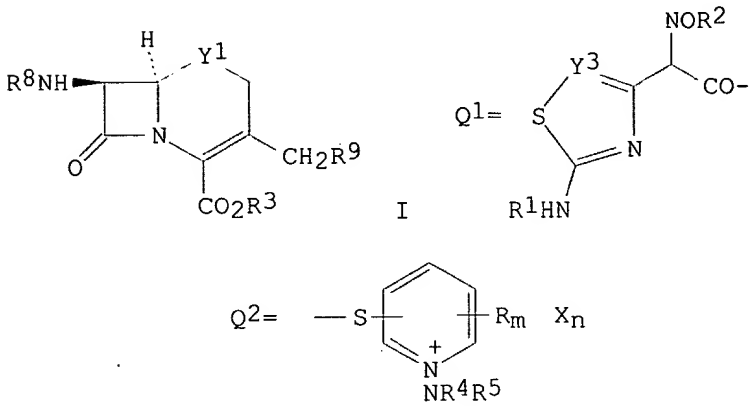
I-

Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



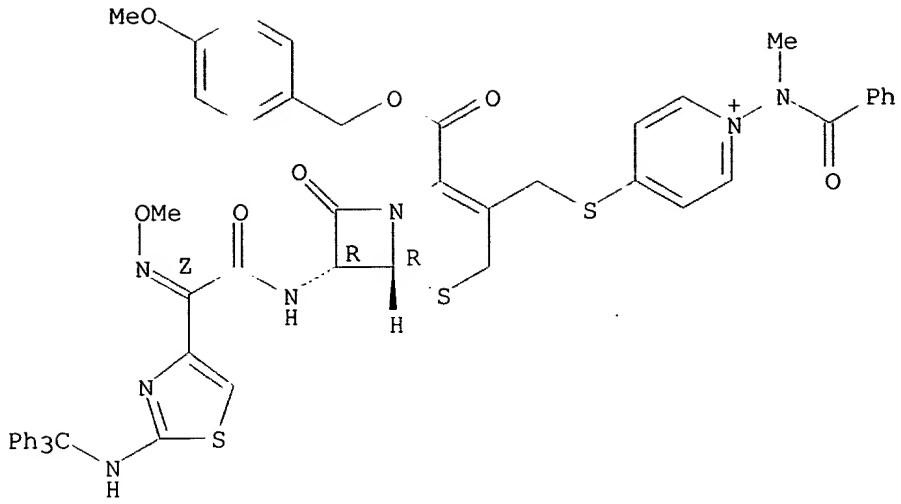
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 10 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-64-7 REGISTRY
CN Pyridinium, 1-(benzoylmethylamino)-4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C54 H48 N7 O7 S3 . I
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



PAGE 2-A

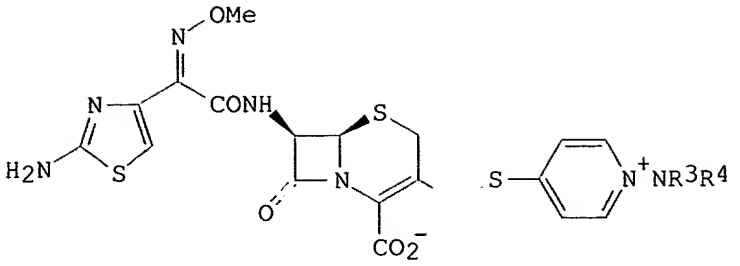
● I^-

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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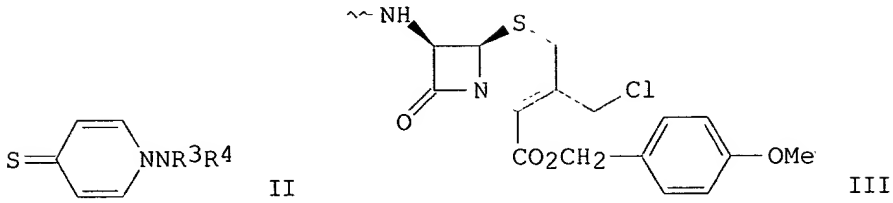

II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

REFERENCE 2: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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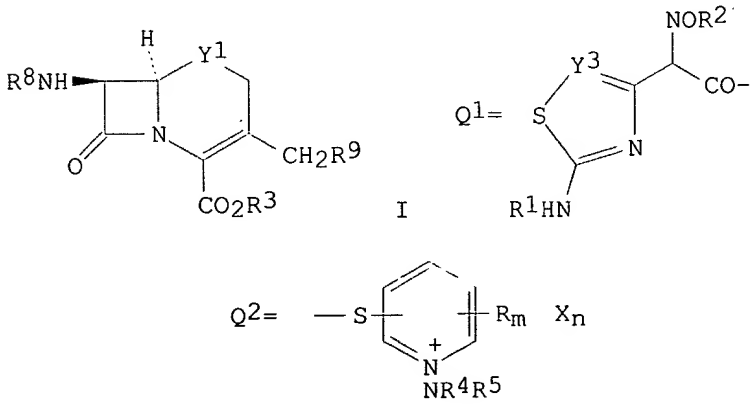


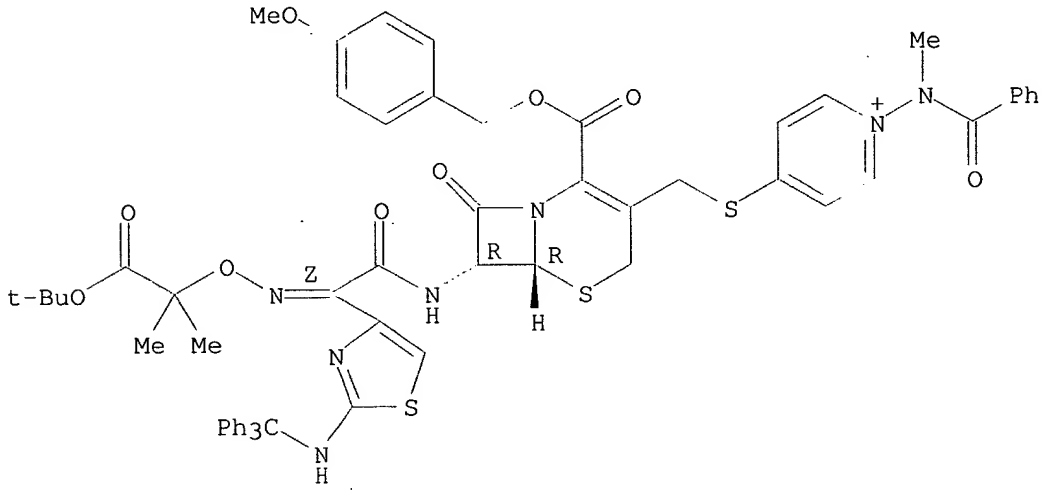
I

AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 =

thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 11 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-63-6 REGISTRY
CN Pyridinium, 4-[[[7-[[[[2-(1,1-dimethylethoxy)-1,1-dimethyl-2-oxoethoxy]imino][2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(benzoylmethylamino)-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C61 H60 N7 O9 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



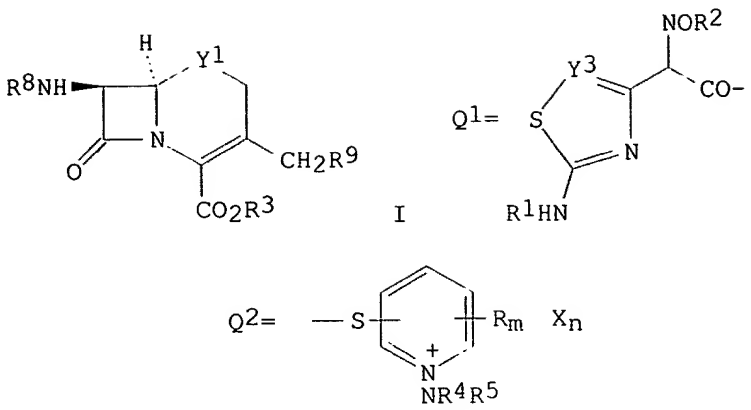
● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

Searched by: Mary Hale 308-4258 CM-1 12D16

GI



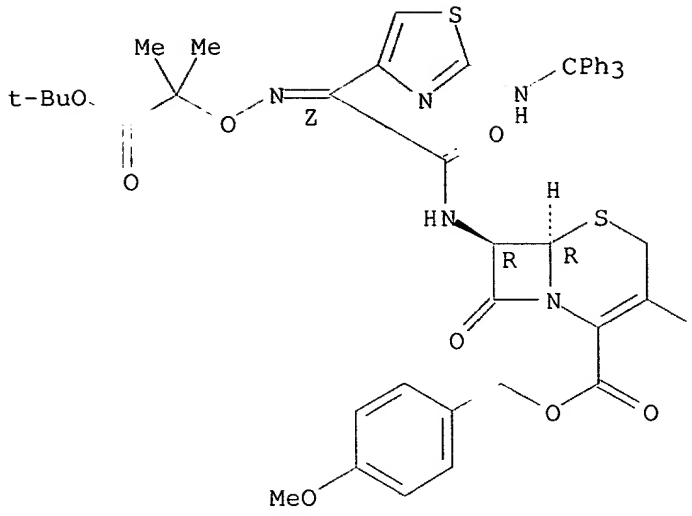
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 12 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-62-5 REGISTRY
CN Pyridinium, 1-[[3,4-bis[(4-methoxyphenyl)methoxy]benzoyl]methylamino]-4-[[[7-[[[[2-(1,1-dimethylethoxy)-1,1-dimethyl-2-oxoethoxy]imino][2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C77 H76 N7 O13 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

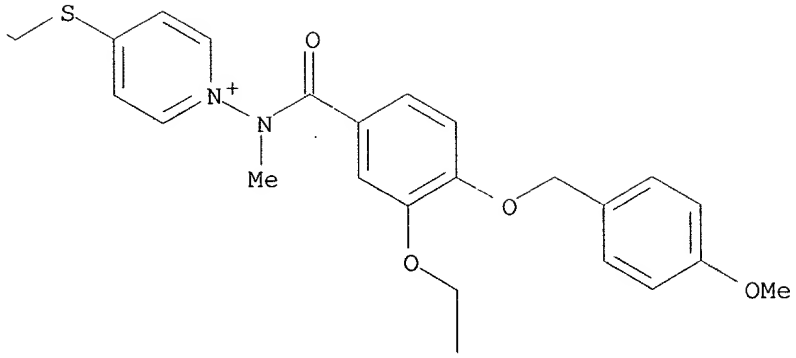
Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A

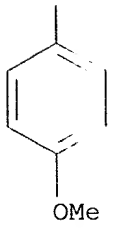


PAGE 1-B



Searched by: Mary Hale 308-4258 CM-1 12D16

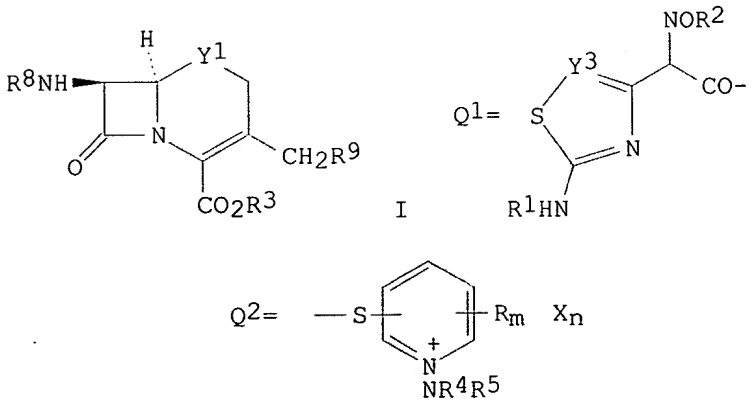
● I^-



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 =

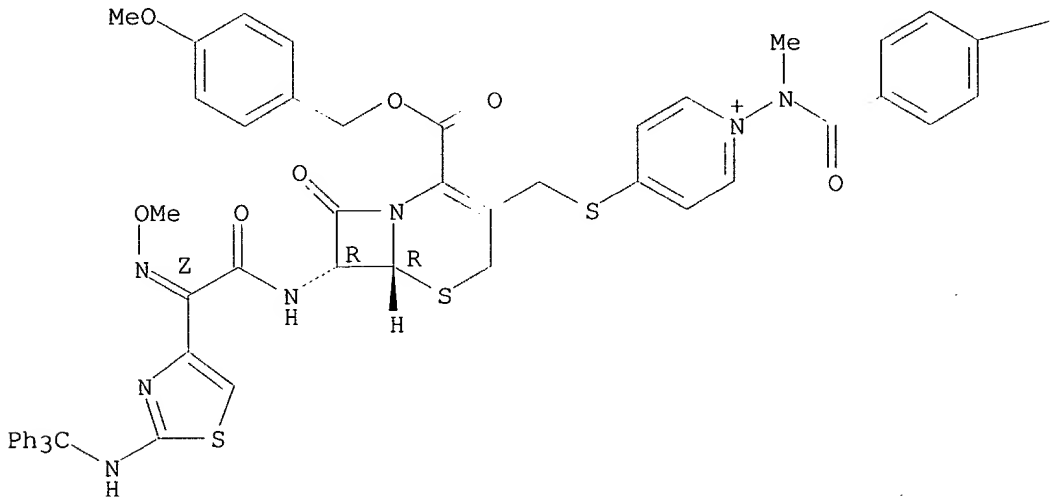
Searched by: Mary Hale 308-4258 CM-1 12D16

thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

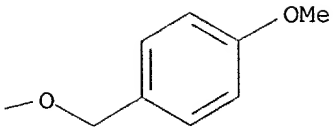
L3 ANSWER 13 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134482-61-4 REGISTRY
CN Pyridinium, 4-[[[7-[[(methoxyimino)[2-[(triphenylmethyl)amino]-4-thiazolyl]acetyl]amino]-2-[[(4-methoxyphenyl)methoxy]carbonyl]-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[[4-[(4-methoxyphenyl)methoxy]benzoyl]methylamino]-, iodide, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C62 H56 N7 O9 S3 . I
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



Searched by: Mary Hale 308-4258 CM-1 12D16

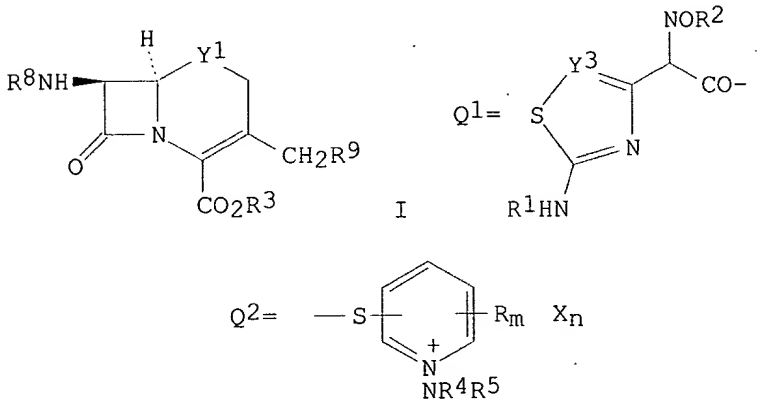


● I^-

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxy lates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI



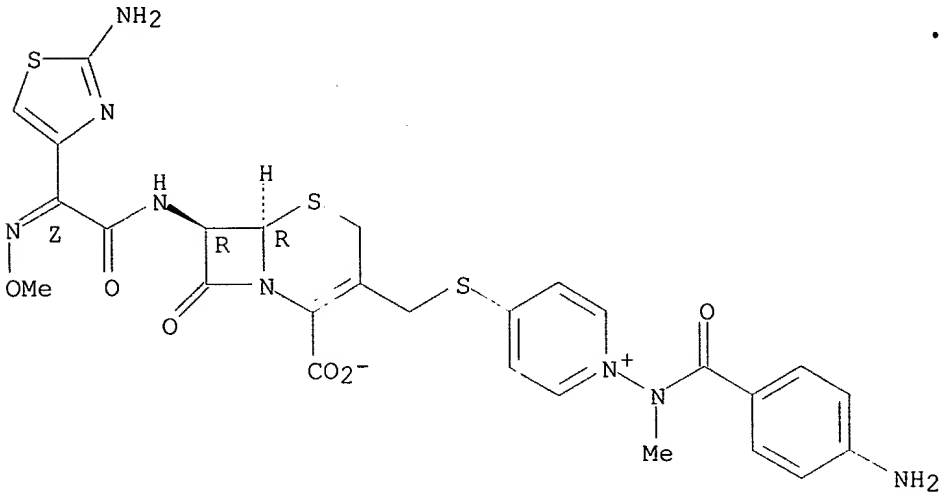
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 14 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-83-7 REGISTRY

Searched by: Mary Hale 308-4258 CM-1 12D16

CN Pyridinium, 1-[(4-aminobenzoyl)methylamino]-4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H26 N8 O6 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

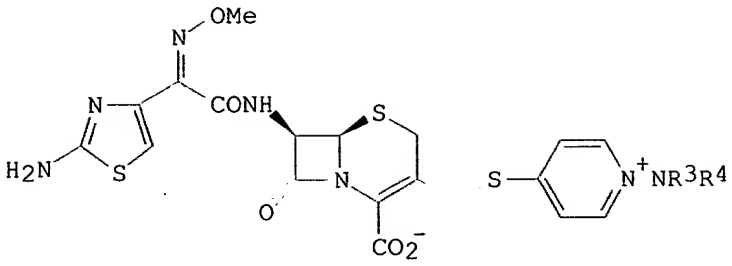
Absolute stereochemistry.
Double bond geometry as shown.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.
GI

Searched by: Mary Hale 308-4258 CM-1 12D16



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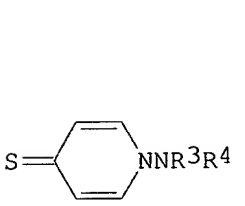

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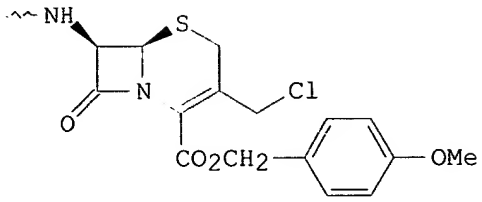

III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

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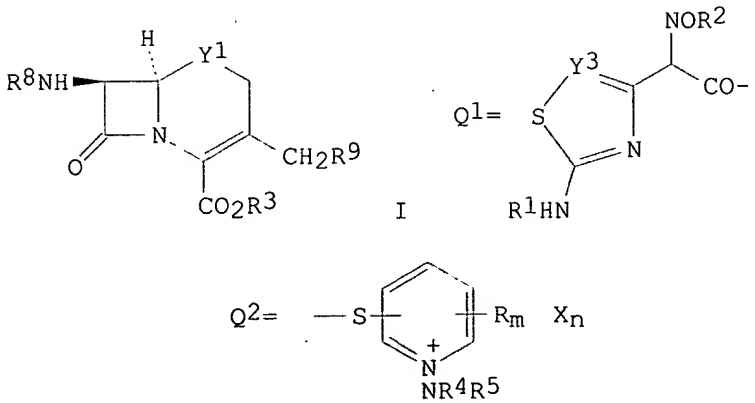


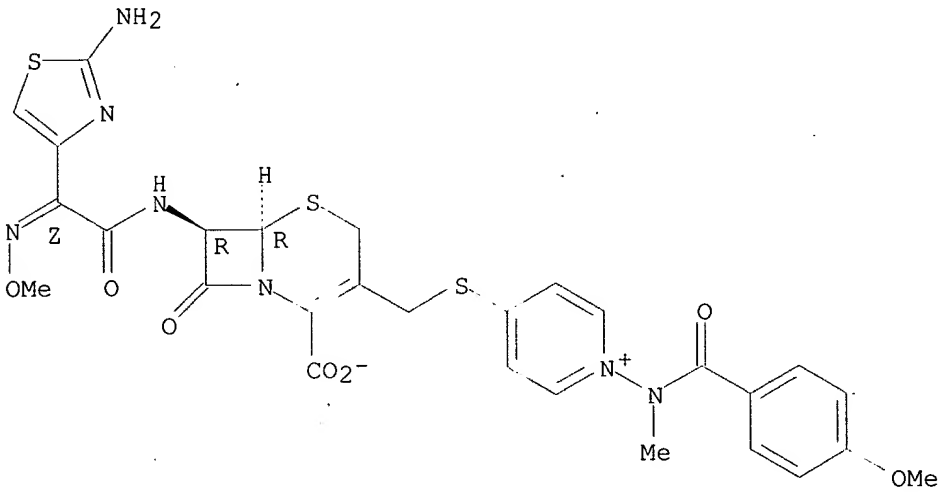
I

Searched by: Mary Hale 308-4258 CM-1 12D16

AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 15 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-76-8 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(4-methoxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C28 H27 N7 O7 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

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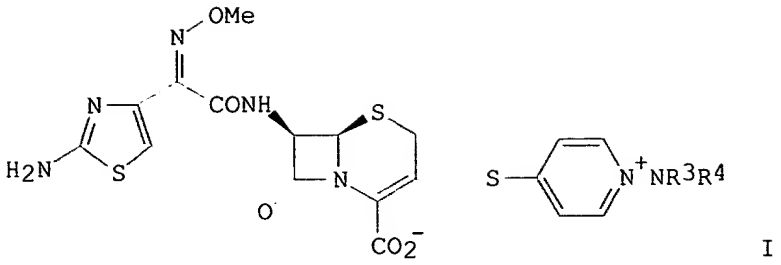
Searched by: Mary Hale 308-4258 CM-1 12D16



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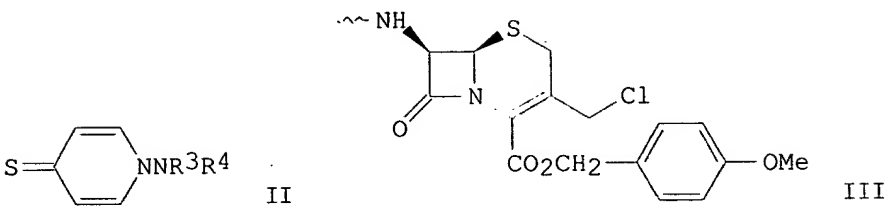

II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

REFERENCE 2: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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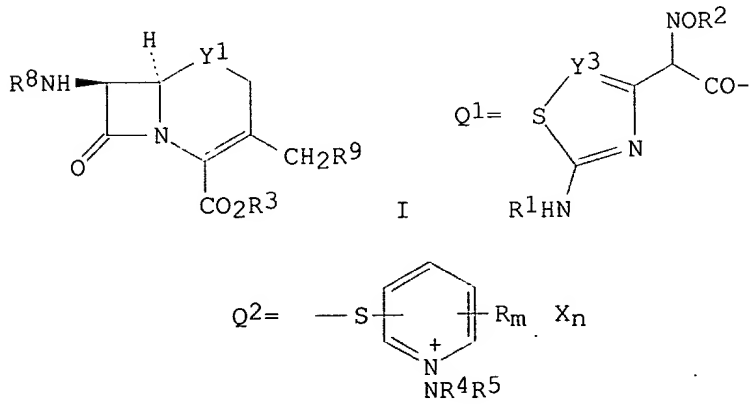


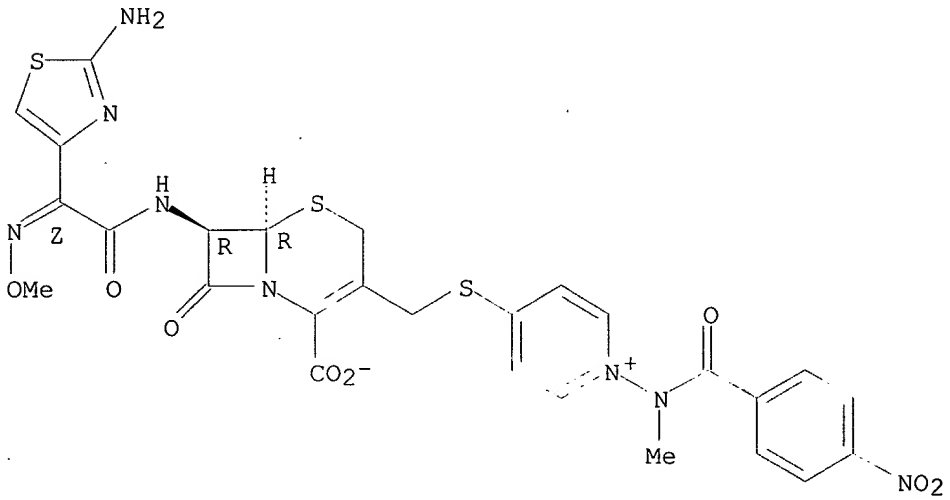
I

Searched by: Mary Hale 308-4258 CM-1 12D16

AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 16 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-75-7 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[methyl(4-nitrobenzoyl)amino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H24 N8 O8 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

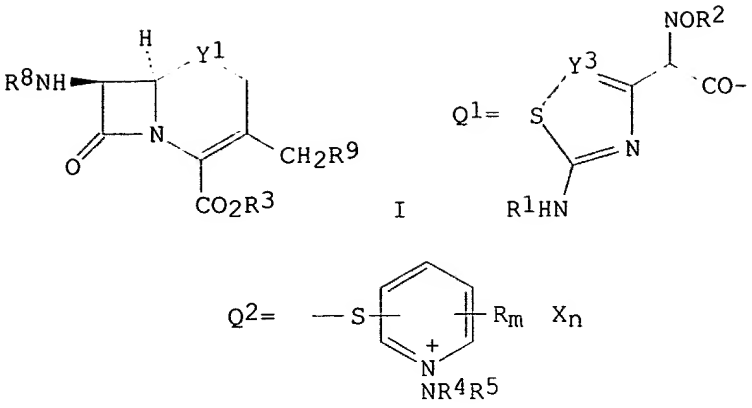


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

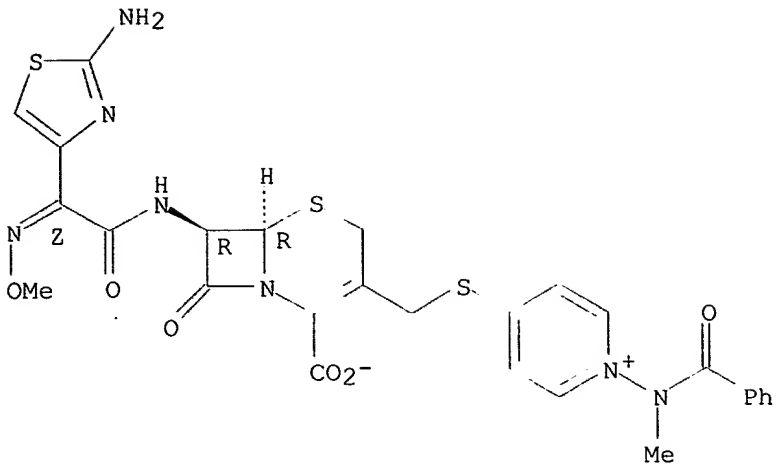


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 17 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-72-4 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(benzoylmethylamino)-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H25 N7 O6 S3
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:163761 Synthesis and biological properties of some 3-[(N-substituted amino)pyridinium-4-thiomethyl]-7-[2-(2-amino-thiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]ceph-3-em-4-carboxylates. Branch, Clive L.; Adams, Richard G.; Brain, Edward G.; Guest, Angela W.; Harrington, Frank P.; Knott, Sarah J.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1289-99 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

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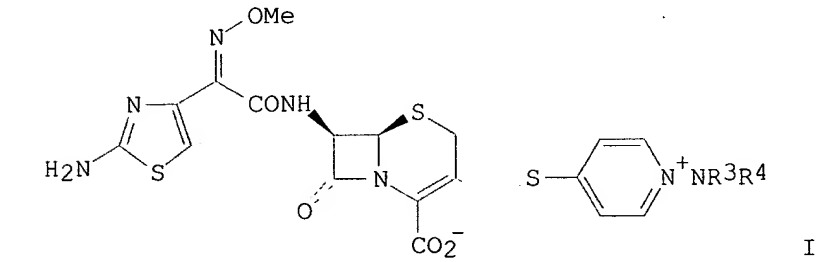

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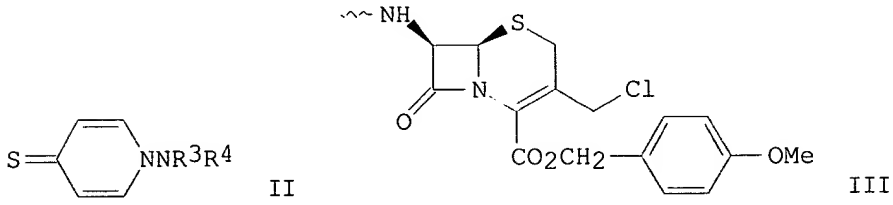

II III

AB The synthesis and antibacterial activity of a series of .beta.-lactamase stable, broad spectrum 7-[2-(2-aminothiazol-4-yl)-2-(Z)-(methoxyimino)acetamido]cephalosporins I (R3 = H, Me, R4 = H, Me, cyclopentyl, CH2Ph, Bz, COC6H4OMe-4, etc.), characterized by a C-3-[N-(substituted amino)pyridinium-4-thiomethyl] group, is described. Thus, alkylation of thiopyridones II with (chloromethyl)cephemcarboxylate III followed by hydrolysis gave I. Gram-pos. and Gram-neg. bacteria

Searched by: Mary Hale 308-4258 CM-1 12D16

including extended spectrum .beta.-lactamase-producing strains were most susceptible to the N-amino- and N-methylamino derivs. I (R3 = R4 = H; R3 = H, R4 = Me); with the exception of Pseudomonas aeruginosa, I (R3 = H, R4 = Me) was more active in vitro and in vivo than cefpirome or ceftazidime.

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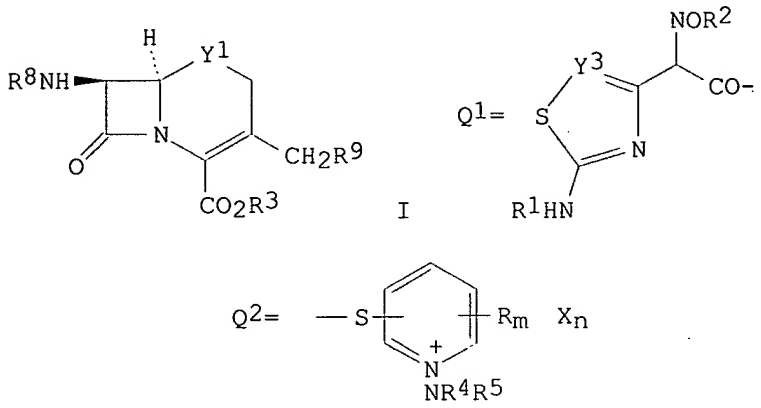
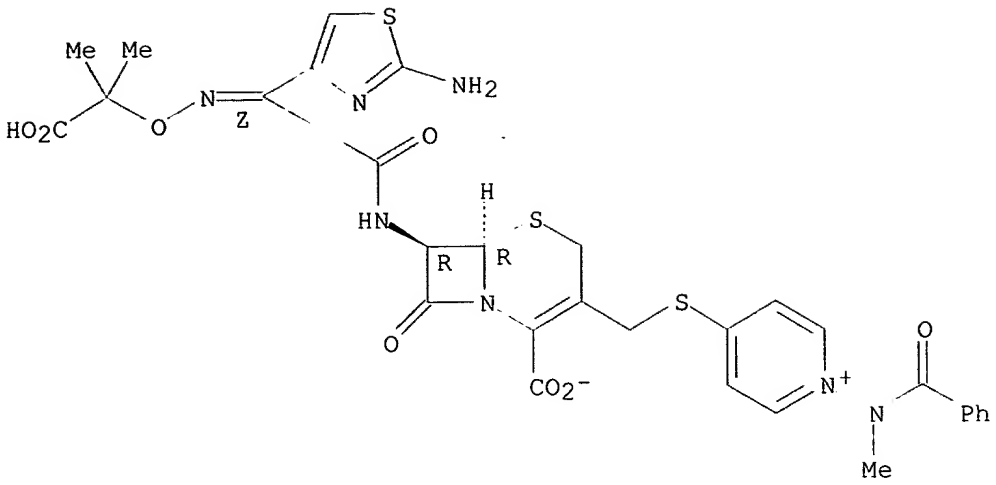


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 18 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-71-3 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(benzoylmethylamino)-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H29 N7 O8 S3
CI COM
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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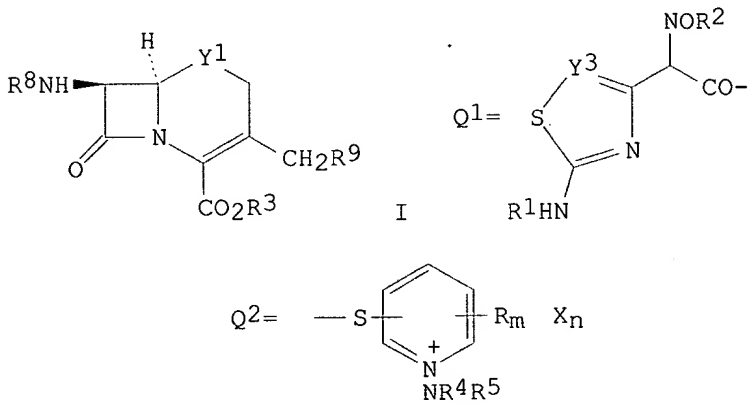


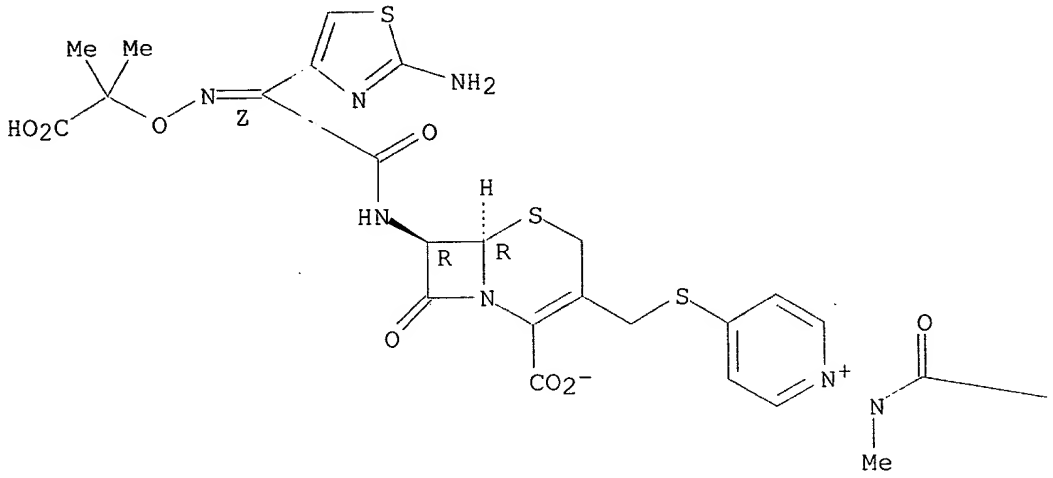
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

Searched by: Mary Hale 308-4258 CM-1 12D16

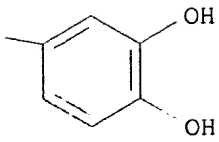
L3 ANSWER 19 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-70-2 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)[(1-carboxy-1-methylethoxy)imino]acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,4-dihydroxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C30 H29 N7 O10 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 1-B



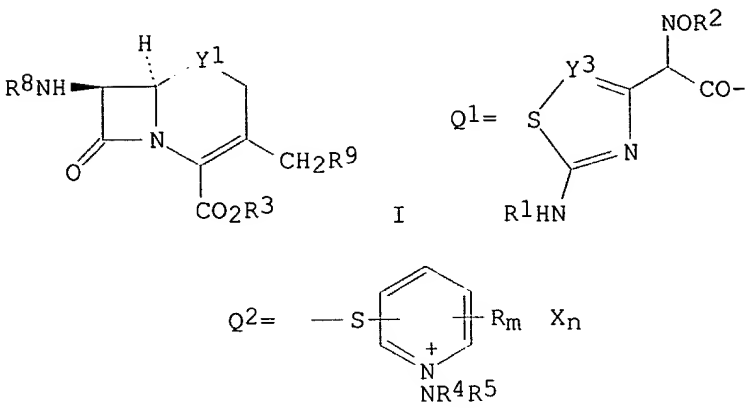
1 REFERENCES IN FILE CA (1967 TO DATE)

Searched by: Mary Hale 308-4258 CM-1 12D16

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxy lates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

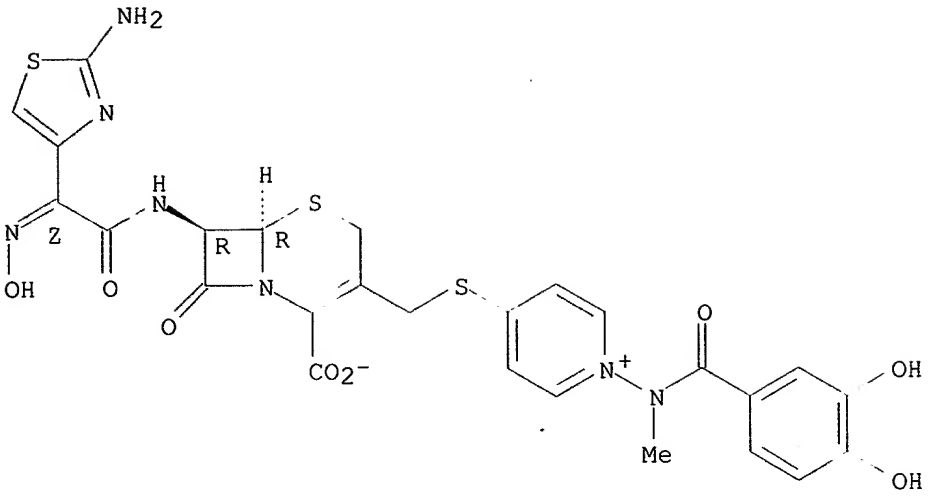


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

L3 ANSWER 20 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-69-9 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(hydroxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,4-dihydroxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C26 H23 N7 O8 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

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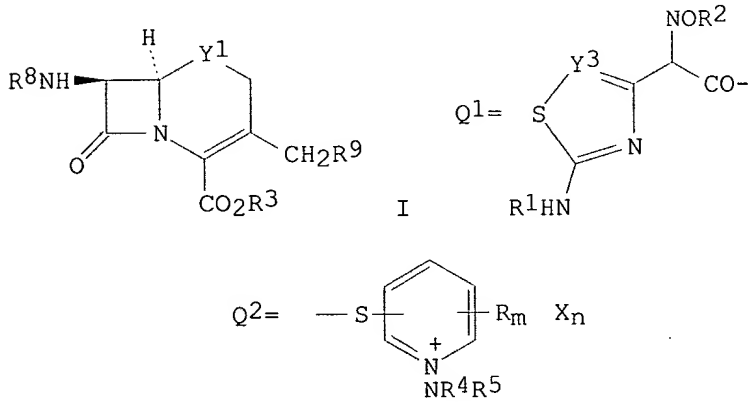
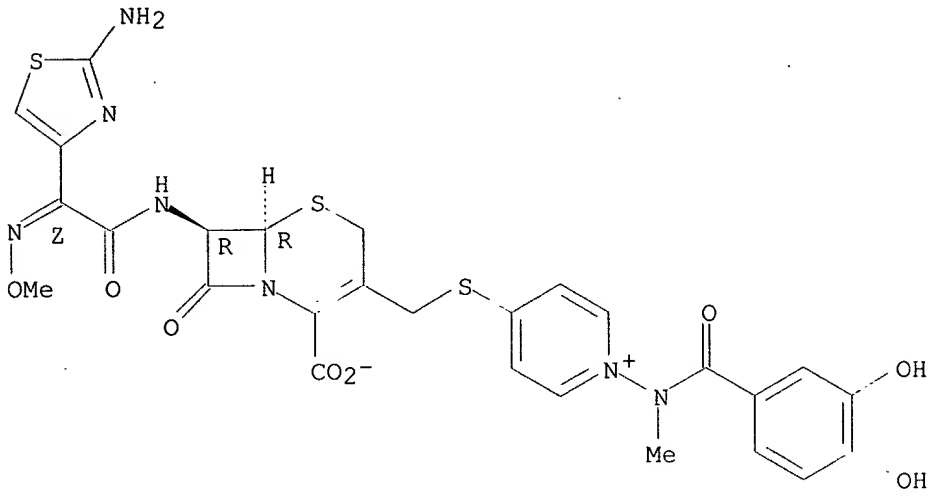


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

Searched by: Mary Hale 308-4258 CM-1 12D16

L3 ANSWER 21 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134481-68-8 REGISTRY
CN Pyridinium, 4-[[[7-[[(2-amino-4-thiazolyl)(methoxyimino)acetyl]amino]-2-carboxy-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,4-dihydroxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(Z)]]-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H25 N7 O8 S3
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.
Double bond geometry as shown.

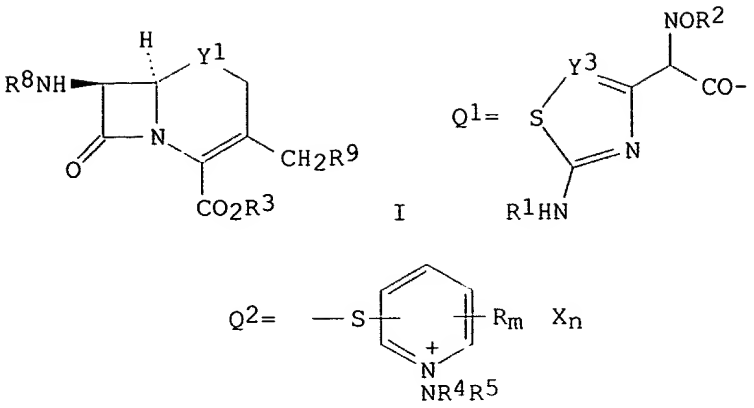


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 116:6335 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Adams, Richard George (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416814 A2 19910313, 93 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309493 19900830. PRIORITY: GB 1989-19945 19890904; GB 1989-19946 19890904; GB 1990-10265 19900508; GB 1990-10299 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

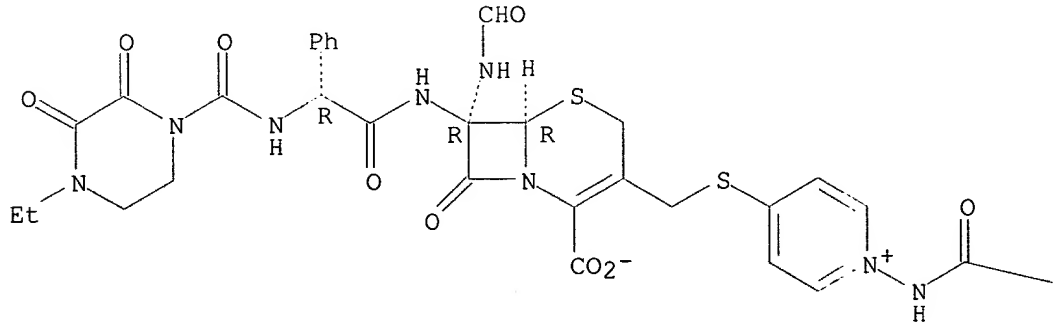


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R8 = thiazolyloximinoacetyl group Q1; R9 = pyridiniumylthio group Q2; R1 = H, amino-protective group; R2 = H, (cyclo)alkyl, (cyclo)alkenyl, alkynyl, aryl, etc.; R4, R5 = H, acyl, (cyclo)alkyl, (cyclo)alkenyl, aryl, etc.; NR4R5 = heterocyclyl, amidine group; R = substituent, X = anion; Y1 = O, SOp, CH2; Y3 = N, CH; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I [R3 = CH2C6H4OMe-4, R8 = Q1, R1 = Ph3C, R2 = Me, Y3 = CH, R9 = iodo] was condensed with 1-(dimethylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R8 = Q1, R1 = H, R2 = Me, Y3 = CH, R9 = 1-(dimethylamino)pyridinium-4-ylthio iodide].

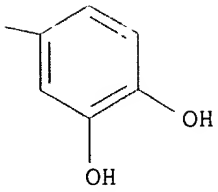
L3 ANSWER 22 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134392-73-7 REGISTRY
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,4-dihydroxybenzoyl)amino]-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C36 H34 N8 O11 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



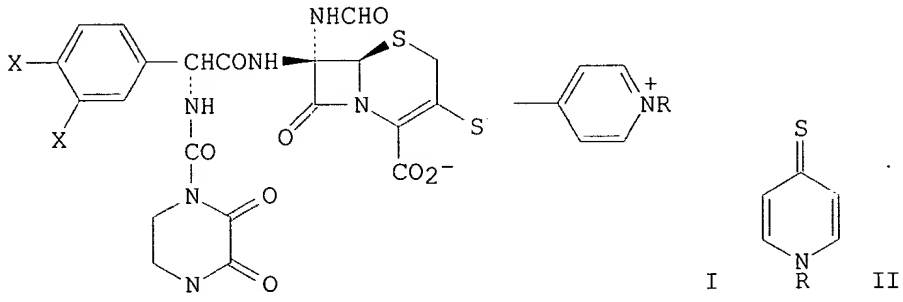
Searched by: Mary Hale 308-4258 CM-1 12D16



2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:134093 Synthesis and biological activity of 3-(N-substituted pyridinium-4-thiomethyl)-7.alpha.-formamidocephalosporins. Guest, Angela W.; Adams, Richard G.; Basker, Michael J.; Brain, Edward G.; Branch, Clive L.; Harrington, Frank P.; Neale, Jane E.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1279-88 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

GI



I II

AB The synthesis and antibacterial activity of a series of 3-(1-substituted pyridinium-4-thiomethyl)-7.alpha.-formamidocephalosporins I (R = Me, CH2CO2H, CH2COMe, 3,4-dihydroxybenzyl, X = H, OH; R = NR1R2, R1 = 3,4-dihydroxybenzoyl, Me, H, R2 = H, Me, X = H, OH) is described. The key step in the synthetic sequence is the prepn. of the thiopyridones II by alkylation of 4-pyridone or condensation reactions with 4-thioxopyrone. All the derivs. showed good potency and stability to bacterial .beta.-lactamases. The antibacterial efficacy seen with the N-alkylpyridinium substituents was enhanced by the introduction of a catecholic side chain at C-7 and by prepn. of N-(substituted amino)pyridinium derivs.

REFERENCE 2: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat.

Searched by: Mary Hale 308-4258 CM-1 12D16

Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

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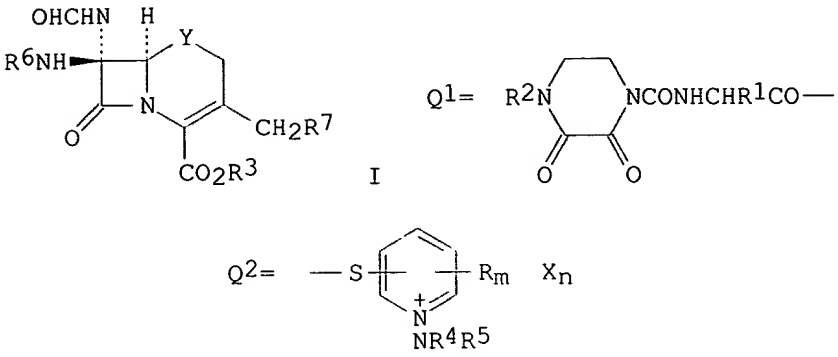


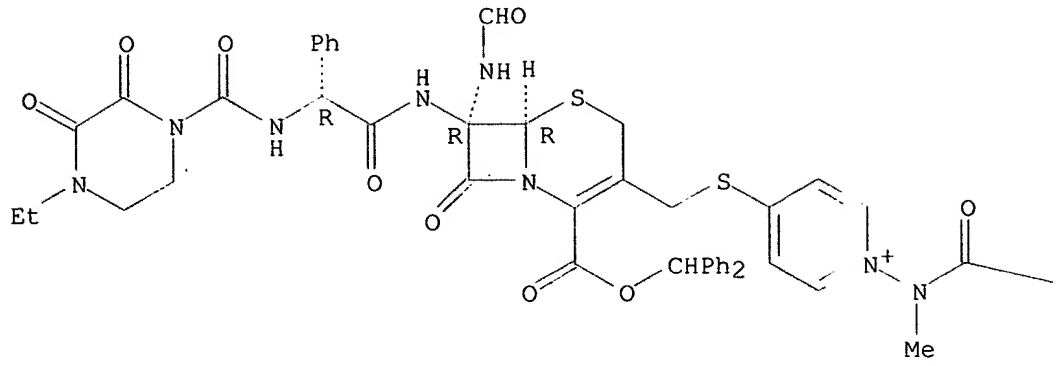
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

L3 ANSWER 23 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134368-52-8 REGISTRY
CN Pyridinium, 4-[[[2-[(diphenylmethoxy)carbonyl]-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(4-methoxybenzoyl)methylamino]-, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C51 H49 N8 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



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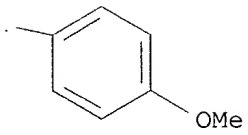
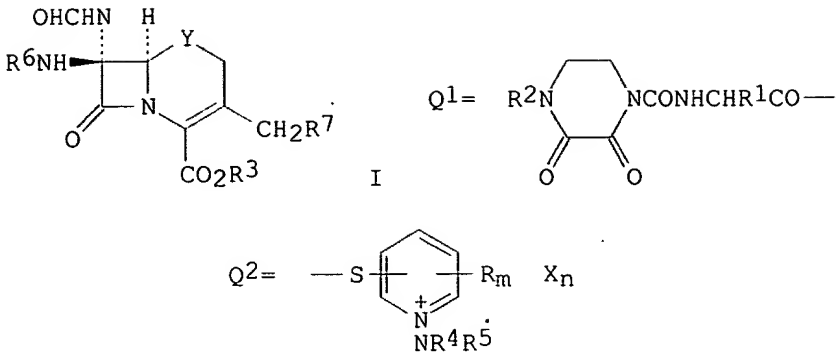


1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

GI

Searched by: Mary Hale 308-4258 CM-1 12D16

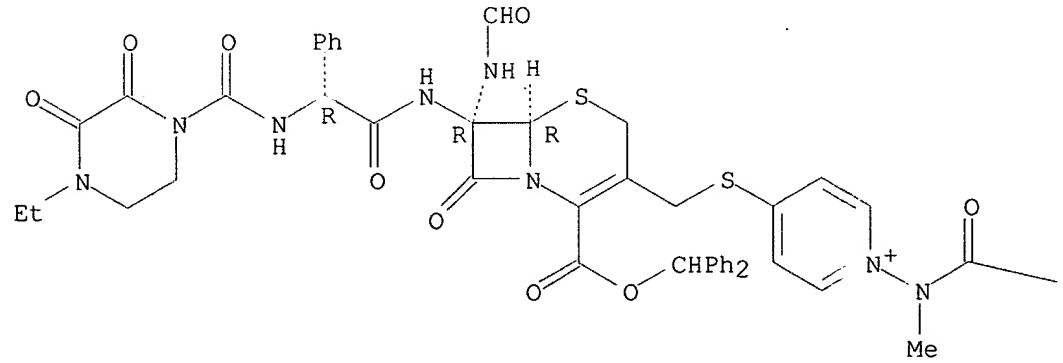


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

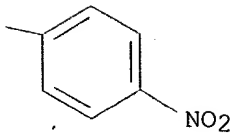
L3 ANSWER 24 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134368-51-7 REGISTRY
CN Pyridinium, 4-[[[2-[(diphenylmethoxy)carbonyl]-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[methyl(4-nitrobenzoyl)amino]-, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C50 H46 N9 O11 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



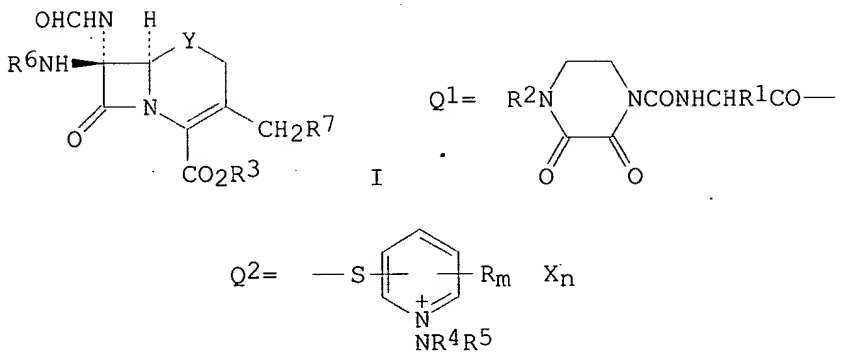
Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

GI



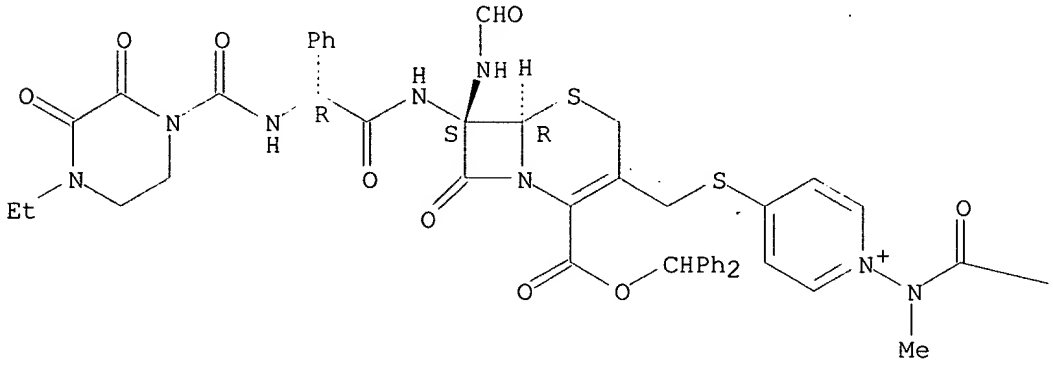
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

Searched by: Mary Hale 308-4258 CM-1 12D16

L3 ANSWER 25 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134368-46-0 REGISTRY
CN Pyridinium, 1-[[3,4-bis[(4-methoxyphenyl)methoxy]benzoyl]methylamino]-4-[[[2-[(diphenylmethoxy)carbonyl]-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, [6R-[6.alpha.,7.alpha.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C66 H63 N8 O13 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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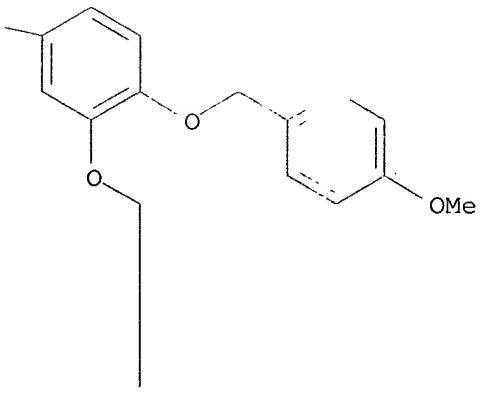
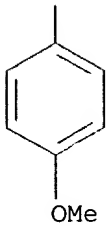


Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

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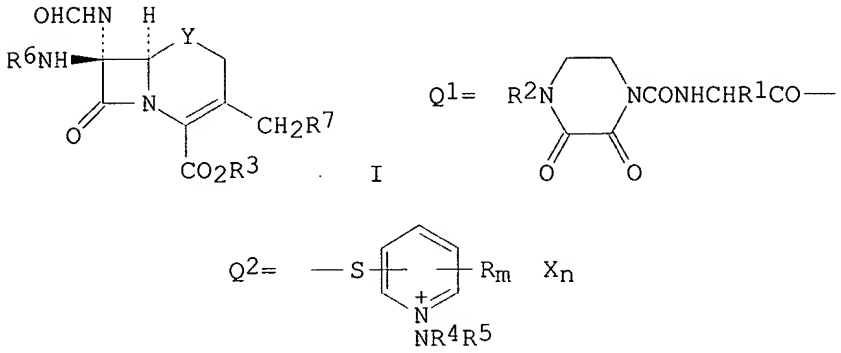
GI



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

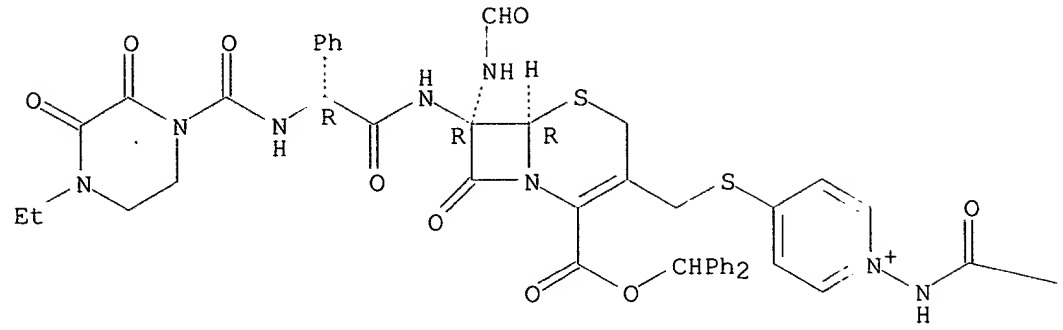
L3 ANSWER 26 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134368-43-7 REGISTRY
CN Pyridinium, 1-[(3,4-dihydroxybenzoyl)amino]-4-[[[2-[(diphenylmethoxy)carbonyl]-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)

Searched by: Mary Hale 308-4258 CM-1 12D16

FS STEREOSEARCH
MF C49 H45 N8 O11 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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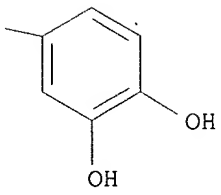

1 REFERENCES IN FILE CA (1967 TO DATE)
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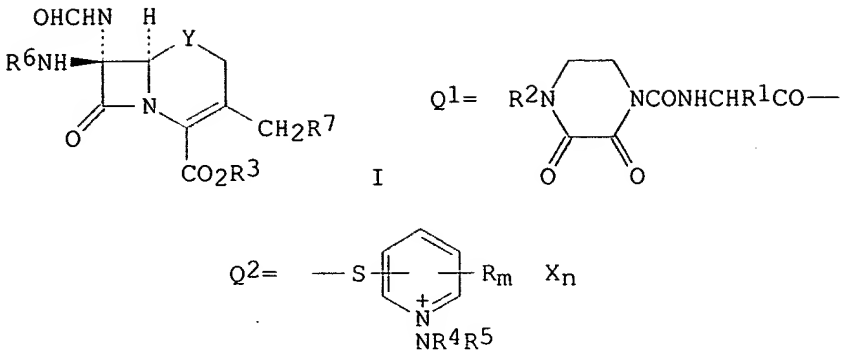
REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

GI

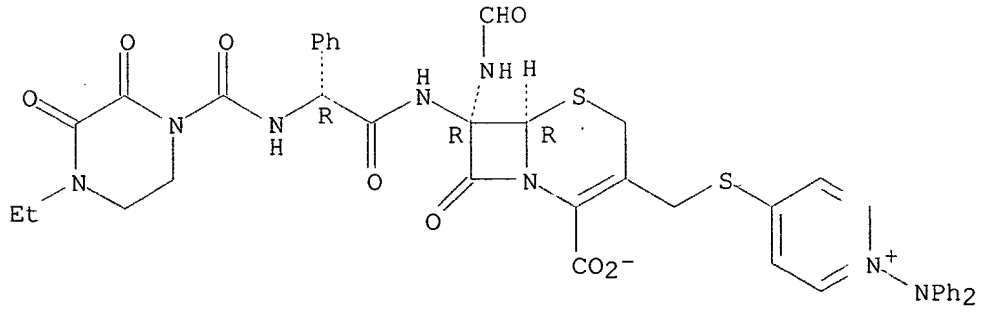
Searched by: Mary Hale 308-4258 CM-1 12D16



AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

L3 ANSWER 27 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134367-97-8 REGISTRY
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-(diphenylamino)-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C41 H38 N8 O8 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH,

Searched by: Mary Hale 308-4258 CM-1 12D16

DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

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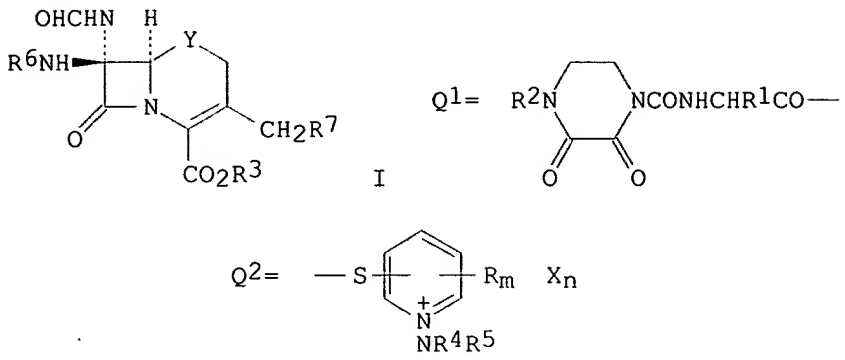


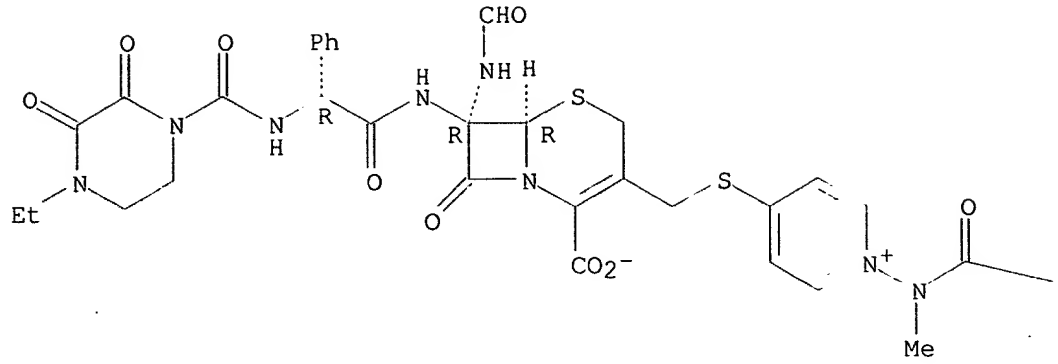
AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

L3 ANSWER 28 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134367-93-4 REGISTRY
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(4-methoxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C38 H38 N8 O10 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

Searched by: Mary Hale 308-4258 CM-1 12D16

PAGE 1-A



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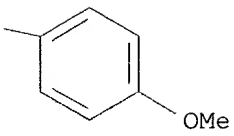

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

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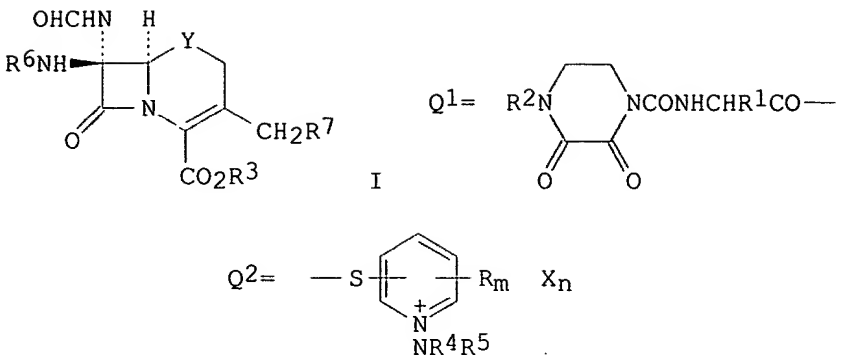
Searched by: Mary Hale 308-4258 CM-1 12D16

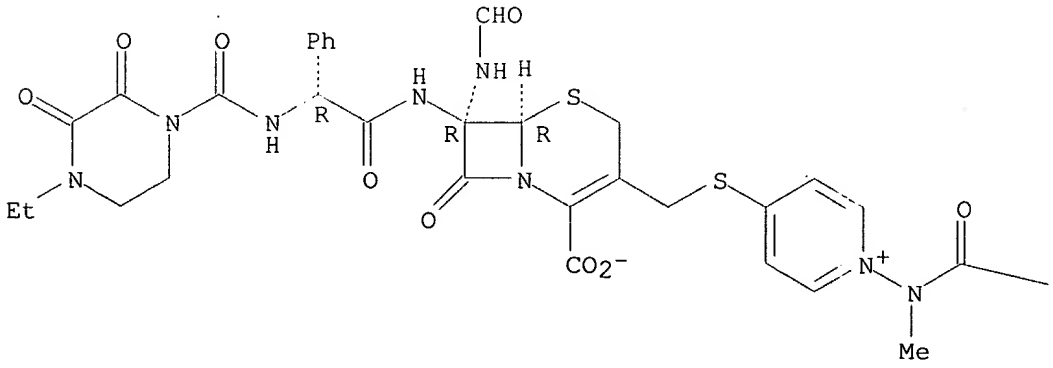


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

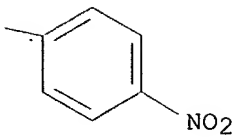
L3 ANSWER 29 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134367-92-3 REGISTRY
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[methyl(4-nitrobenzoyl)amino]-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C37 H35 N9 O11 S2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

PAGE 1-A



Searched by: Mary Hale 308-4258 CM-1 12D16



1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

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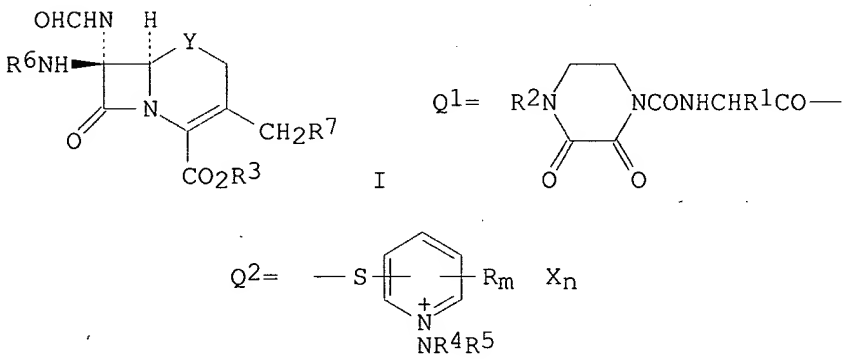


AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

L3 ANSWER 30 OF 30 REGISTRY COPYRIGHT 2002 ACS
RN 134367-87-6 REGISTRY
CN Pyridinium, 4-[[[2-carboxy-7-[[[[(4-ethyl-2,3-dioxo-1-

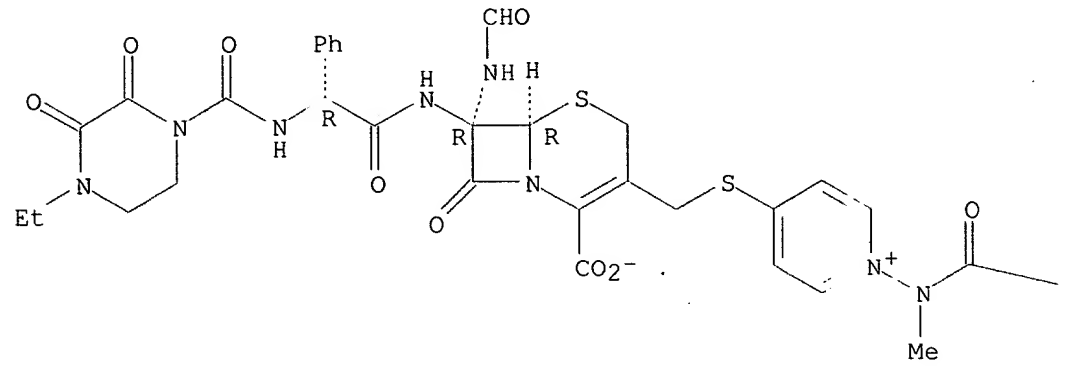
Searched by: Mary Hale 308-4258 CM-1 12D16

piperazinyl)carbonyl]amino]phenylacetyl]amino]-7-(formylamino)-8-oxo-5-thia-1-azabicyclo[4.2.0]oct-2-en-3-yl]methyl]thio]-1-[(3,4-dihydroxybenzoyl)methylamino]-, inner salt, [6R-[6.alpha.,7.beta.(R*)]]-(9CI) (CA INDEX NAME)

FS STEREOSEARCH
MF C37 H36 N8 O11 S2
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

PAGE 1-A



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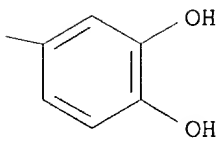

2 REFERENCES IN FILE CA (1967 TO DATE)
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 120:134093 Synthesis and biological activity of 3-(N-substituted pyridinium-4-thiomethyl)-7.alpha.-formamidocephalosporins. Guest, Angela W.; Adams, Richard G.; Basker, Michael J.; Brain, Edward G.; Branch, Clive L.; Harrington, Frank P.; Neale, Jane E.; Pearson, Michael J.; Zomaya, Iskander I. (SmithKline Beecham Pharm., Brockham Park/Betchworth/Surrey, RH3 7AJ, UK). J. Antibiot., 46(8), 1279-88 (English) 1993. CODEN: JANTAJ. ISSN: 0021-8820.

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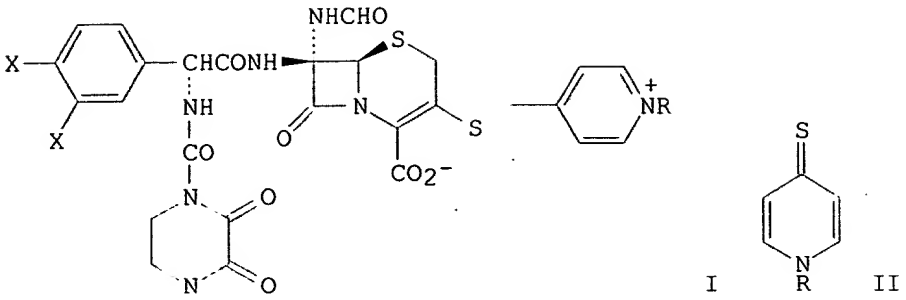
Searched by: Mary Hale 308-4258 CM-1 12D16



I II

AB The synthesis and antibacterial activity of a series of 3-(1-substituted pyridinium-4-thiomethyl)-7.alpha.-formamidocephalosporins I (R = Me, CH2CO2H, CH2COMe, 3,4-dihydroxybenzyl, X = H, OH; R = NR1R2, R1 = 3,4-dihydroxybenzoyl, Me, H, R2 = H, Me, X = H, OH) is described. The key step in the synthetic sequence is the prepn. of the thiopyridones II by alkylation of 4-pyridone or condensation reactions with 4-thioxopyrone. All the derivs. showed good potency and stability to bacterial .beta.-lactamases. The antibacterial efficacy seen with the N-alkylpyridinium substituents was enhanced by the introduction of a catecholic side chain at C-7 and by prepn. of N-(substituted amino)pyridinium derivs.

REFERENCE 2: 115:8422 Preparation of 3-(pyridiniumylthiomethyl)cephemcarboxylates and analogs as antibiotics. Branch, Clive Leslie; Guest, Angela Wendy; Finch, Stephen Christopher (Beecham Group PLC, UK). Eur. Pat. Appl. EP 416810 A2 19910313, 63 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1990-309483 19900830. PRIORITY: GB 1989-19944 19890904; GB 1990-10264 19900508.

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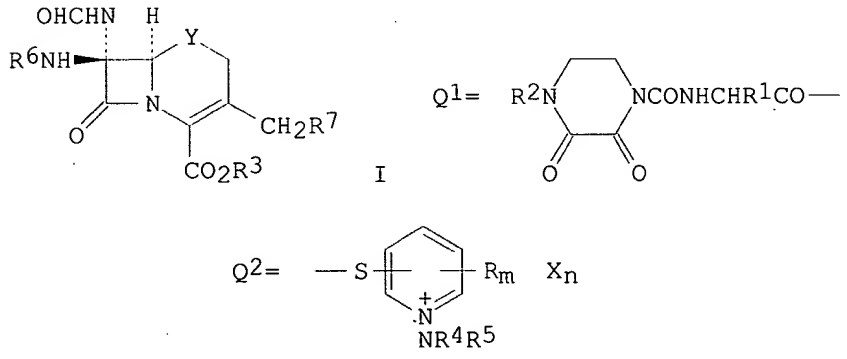

I

AB The title compds. [I; R3 = H, neg. charge, carboxy-protective group; R6 = dioxopiperazinylcarbonylaminoacetyl group Q1; R7 = pyridiniumylthio group Q2; R1 = cyclohex(adi)enyl, CHMeOH,CH2CH2SMe, (un) substituted Ph, heterocyclyl; R2 = alkyl; R = substituent; R4,R5 = H (un)substituted (cyclo)alkyl, (cyclo)alkenyl, alkanoyl, etc.; NR4R5 = heterocyclyl, amidine group; X = anion; Y = O, SOp, CH2; m = 0-4; n = 0,1; p = 0-2] were prepd. as antibiotics (no data). Thus, I (R = CHPH2, R6 = H, R7 = Br) was condensed with (R)-Q1OH (R1 = Ph, R2 = Et) and the product condensed with 1-(3,4-dihydroxybenzoylamino)-4-thiopyridone (prepn. given) to give, after

deprotection, I [R3 = neg. charge, R6 = (R)-Q1, R1 = Ph, R2 = Et, R7 = 1-(3,4-dihydroxybenzoylamino)pyridinium-4-yl thio].

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	258.40	1269.20

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-17.70	-37.64

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FILE COVERS 1907-1966
FILE LAST UPDATED: 01 May 1997 (19970501/UP)

This file contains CAS Registry Numbers for easy and accurate substance identification. Title keywords, authors, patent assignees, and patent information, e.g., patent numbers, are now searchable from 1907-1966. TIFF images of CA abstracts printed between 1907-1966 are available in the PAGE display formats.

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